THE RELATIVE MERITS OF VARIOUS SUTURE MATERIALS FOR THE REPAIR OF SEVERED NERVES.

By S. SUNDERLAND and G. K. SMITH.

Department of Anatomy and Histology, University of Melbourne.

INTRODUCTION.

EXPERIMENTAL investigations undertaken to determine the relative merits of different suture materials for repairing severed nerves have been concerned with the extent and quality of the reaction which each induced and the possible effects of this reaction on regeneration. A review of these earlier experiments reveals that they were incomplete in certain particular respects. In Guttmann's (1943) experiments, for example, the nerves were divided for the purpose of the investigation which meant that the reaction to the material employed to execute the repair was examined in traumatised tissue; as a preliminary to severance some of the nerves were also crushed over a distance of 10 mm. Admittedly these experimental conditions resemble those under which the suture would normally be required and used but under such conditions the response to the suture material could be obscured by and confused with (I) the reaction provoked by the injury and aggravated by the manipulation of the nerve ends while effecting union and (II) the changes associated with the natural processes of repair; these present individual peculiarities and may reach considerable proportions. As a result misinterpretations may arise as to the amount of the reaction directly attributable to the presence of the suture. In the experiments referred to, no consideration was given to this complicating factor, with the result that

the effect of individual suture materials on peripheral nerve tissue has by no means been convincingly established by those studies.

Secondly, exposing and mobilising the nerve and passing a needle and suture material completely through it could, no matter how delicately these procedures are performed, conceivably excite a reaction which could contribute to the condition observed when the suture material has been left *in situ*. Unless the changes attributable to this common factor are excluded by the use of appropriate controls the extent to which it may confuse the issue remains unknown.

Thirdly, while the early reaction has in the past received considerable attention, the residual reaction has, on the contrary, been rather neglected. The duration of the experiment exceeded twenty-six days in 3 of Sargent and Greenfield's (1919) series of 9 experiments and in only 3 of Guttmann's (1943) series of 36. Tarlov *et al.* (1948), however, in their comparative studies on plasma clot and black silk sutures followed the sequence of events subsequent to repair for periods up to four hundred and seventeen days.

Having in mind these limitations a further set of experiments was designed to isolate and assess the early and late reaction of the host tissues to the implanted foreign body in order to determine the suture material

which provokes the minimal reaction and introduces the least obstacle to regeneration. The opportunity has been taken to investigate also the properties of some suture materials that were not included in previous studies while the combined use of a variety of suture materials in the same experimental animal has permitted an estimate of the reaction to different materials in the one animal.

MATERIAL AND METHODS.

Thirty-nine experiments were performed and the suture materials and nerves selected for investigation are given in Table I. The common Australian opossum, *Trichosurus vulpecula*, was used for the experiments. Under chloroform anaesthesia the nerve was exposed on each side under aseptic conditions. The hair was removed and the skin prepared with iodine. Following the skin incision only normal saline was used. A small round-bodied atraumatic needle was used for carrying the suture material. On one side the needle and suture material were drawn obliquely through the nerve and the suture tied lightlty so as to avoid destruction or constriction of the nerve. On the control side the needle and suture material were drawn completely through the nerve, by repeating as closely as possible the technique used when the suture was left *in situ*.

Single and multi-funiculated nerves were selected for study. The suture was passed through the funiculi in some and between them in others. In this way it was possible to study the reaction when the thread was entirely extra-funicular, when it had traversed a bundle and when the perineurium had been breached with minimal needle trauma to the subjacent nerve fibres. Bearing in mind the observed range of variation in the reaction to needle trauma it seems reasonable to conclude that, under the conditions of the investigation, the differences observed in the histological reaction could be ascribed to the different suture materials employed.

The wounds were closed, swabbed with iodine and covered with collodion. With one exception they healed by primary intention. Twenty-nine of the experiments were terminated after an interval of twenty-one days while in a second group of 10 the involved area was left undisturbed for one hundred and seventeen days. The nerves were then exposed, the local reaction studied and a segment of nerve containing the involved area removed. Unfortunately we failed to appreciate the full extent of the proximo-distal spread of the reaction with the result that the segments removed for examination were, in many cases, too short to trace the full extent of the reaction up and down the nerve. Each segment was fixed in 10 per cent. formalin, embedded in paraffin, serially sectioned at 15 μ and the sections stained with haematoxylin and eosin and with Van Gieson.
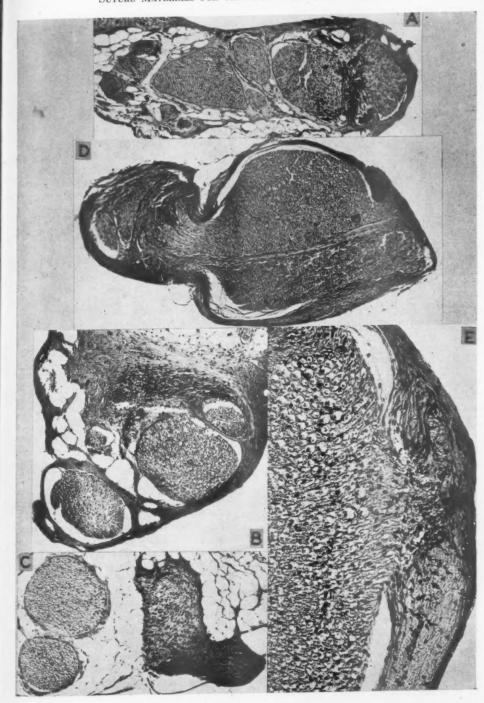
Transverse sections of each nerve in the uninvolved zones above and below the suture together with sections of the segment of the nerve at the site of maximal reaction were enlarged 25 times on a microprojector and drawn. The cross-sectional area of the nerve and its component funiculi were measured on these diagrams by means of a planimeter. Though the nerve tissue and the fibroblastic and cellular reaction often overlapped at the suture site they were occasionally confined predominantly to a particular part of the section. When this occurred it was possible to calculate approximately the cross-sectional areas occupied by each of these tissues. From cross-sectional analyses of the nerve at these three levels it was often possible to express metrically the extent of the reaction in respect of each suture and to correlate this information with the proximo-distal spread of the cellular and fibroblastic response.

Representative muscles innervated by the nerves selected for investigation were removed, weighed and examined histologically for signs of denervation atrophy.

FIG. I. Five photomicrographs from control specimens to illustrate the nature and extent of the reaction induced in a nerve in continuity by the passage of a needle through it. At twenty-one days (A) and at one hundred and seventeen days (B, C, D and E). The "cellular" and fibroblastic reaction which developed along the needle track has remained as a permanent effect. The consequences of an injury sustained in this way were more serious when the funiculi were directly involved during the passage of the needle. (Illustrated on next page.)

Cell types observed in the area of reaction:

In general two types of reaction to the implanted suture material were observed: (a) a cellular response characterised by the presence of the following identified elements: polymorphonuclear leucocytes, lymphocytes, histiocytes, foreign body giant cells and, in the case of silk, plasma cells; (b) a proliferation of fibroblasts originating in the extra-funicular areolar tissue and, when a funiculus was traumatised, in the perineurium and endoneurium. For convenience and to avoid repetition these two types of reaction will be referred to simply as "cellular" and "fibroblastic." In the tables these have been designated "C" and "F" and the severity of the reaction has been expressed as follows: C1, C2, C3, C4 and C5 = a negligible, slight, medium, marked, and massive cellular response respectively; F1, F2, F3, F4 and F5 = a negligible, slight, medium, marked, and massive fibroblastic reaction respectively.

ILLUSTRATIONS.

An attempt has been made to present all illustrations at the same magnification in order to facilitate a comparison of the extent of the reaction set up by the different suture materials. For this scheme to be effective, however, the illustrations of some sections must inevitably be small in order that larger sections could be reproduced at the same magnification. The sections illustrated in figs. III, IV, V, VII, X, XIV, XV, XVI, XVIII and XX are all at the same magnification. The sections illustrated in figs. II, VI, VIII, IX, XII, XIII, XVII, XIX, XXI, and XXII, however, could not be reproduced at the same magnification but had to be slightly reduced in order to include them. A magnification scale has been provided for figs. II to XXII.

OBSERVATIONS.

In the experiments on the median and ulnar nerves no signs of motor disability could be detected during the entire post-operative period and the animals appeared to use the involved limbs quite normally. This suggested that injury to nerve fibres in placing the suture and/or as a result of the reaction to the implanted suture material had been negligible. This was confirmed by the histological examination of nerves and of representative muscles taken at autopsy from the fields of the involved nerves.

THE NATURE OF THE REACTION IN THE CONTROL SPECIMENS IN WHICH THE NEEDLE AND THREAD WERE PASSED THROUGH THE NERVE.

When the needle and suture were drawn through the nerve between the bundles composing it, a fibroblastic reaction developed along the track taken and the adjacent bundles were infiltrated with cells though this response was a mild one (Fig. IA). Sometimes, however, the most delicate handling of the nerve was sufficient to promote a marked cellular reaction inside the funiculi even when these were not directly involved by the passage of the needle and thread. This intra-funicular reaction apparently subsides without leaving any permanent changes but signs of the epineurial reaction were still evident at one hundred and seventeen days in the form of local scarring along the track taken by the needle (Fig. IB).

When the bundles were pierced more severe changes were observed (Figs. IC, D, E). Small funiculi were either grossly distorted or their outlines obscured by the cellular and fibroblastic response which developed as a result of the trauma. However, because this reaction was so sharply localised only small bundles were overwhelmed in this way and an examination of serial sections showed that distally these emerged from the traumatised area with little damage to the contained fibres. The fibres showing Wallerian degeneration were those directly damaged by the needle and these represented only a small proportion of those contained in the punctured funiculus. Thus, despite the fact that the outlines of the bundles were obliterated by the reaction, there was nothing to suggest that this reaction had embarrassed large numbers of nerve fibres. In some specimens scarring through and about the funiculi involved in this way was visible one hundred and seventeen days after the operation which indicates that the early intra-funicular changes may persist (Figs. IC, D, E).

Since the reaction to the passage of the needle and thread was sharply localised the larger bundles retained their essential outlines but presented certain changes at the site where they had been pierced. The subjacent fibres herniated through the defect created in the perineurium and externally became involved in a local cellular reaction which later (one hundred and seventeen days) became converted into a scarred area. Inside the bundle the track of the needle became permanently outlined by a sharply delineated line of scar tissue, beyond which there was no other significant change within the bundle (Fig. ID). Herniations, however, embarrass the fibres involved and, though the reaction and damage were confined to the needle track, the involvement of the conducting elements was much greater and the consequences of the trauma more serious.

It is clear from these studies that the mere passage of the needle and thread through the nerve is sufficient to excite a reaction which, though apparently not affecting fibres in continuity, would certainly present an obstacle to the regeneration of those fibres which had been directly damaged in the experiment.

PLAIN CATGUT.

Early changes at twenty-one days (Figs. II, III, IV):

The nerve was swollen at the site of implantation. The extent of this swelling varied from specimen to specimen, ranging from 2 to 6 times the normal size of the nerve. The suture material was still present but was in the process of disintegration. The characteristic features of the reaction to plain gut were a tremendous cellular response about the suture itself, in which lymphocytes predominated, and external to this a very thin limiting layer of fibroblasts which represented the early stages of encapsulation.

When the suture was confined to the epineurium the small and immediately adjacent bundles were engulfed in the reaction so that all traces of them were lost at the site of implantation (Fig. IV). Those bundles whose outlines were preserved showed a mild diffuse cellular infiltration with some thickening of the perineurium.

FIG. II. Transverse sections of a median nerve illustrating the great cellular reaction produced by the insertion of plain catgut twenty-one days previously. (A) Just above the site of implantation where the mass of tissue resulting from the reaction is situated external to the funiculus. The degree of encapsulation present at twenty-one days is shown. (B) Where the perineurium and subjacent part of the bundle were pierced by the suture. Though the bundle is infiltrated with cells the cellular reaction is concentrated about the suture and the mass of tissue which has developed possesses a definite capsule on its funicular aspect but a thin, poorly-defined capsule elsewhere.

When a bundle was transfixed by the suture the consequences depended on the size of the bundle and the manner in which

the suture had traversed it. The fibroblastic reaction, however, appeared to be more marked than when the epineurium alone was involved, the injured perineurium and endoneurium obviously contributing to the increased fibroblastic response. Smaller bundles were completely submerged by the cellular and fibroblastic reaction. When large funiculi were penetrated their outlines were preserved but they became involved in a reaction which took one of two forms. In the first the break in the perineurium was plugged by the reaction so that there was no herniation of the contents (Fig. II). The large cellular mass which developed about the suture external to the bundle was limited by only a very fine fibroblastic capsule. At the site where this reaction and the suture extended into the funiculus there was a greater admixture of fibroblasts and the entire mass was walled off from the remaining contents of the bundle by a well-defined layer of fibroblasts. There was no

FIG. III. Transverse section of an ulnar nerve twenty-one days after the implantation of plain cat-gut during which the perineurium of the single bundle comprising the nerve was ruptured. The cellular mass which has developed about the suture is joined to the bundle by a band of tissue in which fibroblasts and herniated nerve fibres predominate.

tendency for the cells to invade that portion of the bundle not occupied by the suture which showed surprisingly little change; where the perineurium was not directly involved it showed only a slight thickening.

In the second type of change the intra-funicular reaction about the suture was again confined to the segment directly involved and was rich in fibroblasts. This area was joined to the main cellular mass about the suture external to the bundle by a mass of fibroblasts and herniated nerve fibres which were directed through the break in the perineurium (Fig. III). In other words there was a connecting strand of tissue composed predominantly of fibroblasts and nerve fibres which was interposed between the nerve fibres within the bundle and a large cellular mass externally. The arrangement of these tissues suggested that the reaction was proceeding in a direction away from the nerve despite the fact that the perineurium had been breached.

The fate of the nerve fibres contained in the involved funiculi and particularly in those whose characteristic architectural features were completely obliterated by the reaction will be discussed later. The degeneration of fibres was, however, confined to those directly traumatised; the submergence of fibres in a cellular mass appeared to have no effect on nerve function.

Late changes at one hundred and seventeen days (Fig. V):

In the late stages the nerve at the site of implantation was either not thickened or only slightly so. The suture material had been absorbed and the marked cellular reaction which was such a characteristic feature of the early picture was absent. The fibroblastic changes, which were slight in the early stages, remained. In the epineurium only a slightly denser connective tissue marked the site of implantation. The fibroblastic response was more intense when the bundles had been breached but in these cases the funicular outlines, even those of small bundles, were preserved.

The early and residual pictures suggested that the marked cellular response in the early stages was concerned with the removal
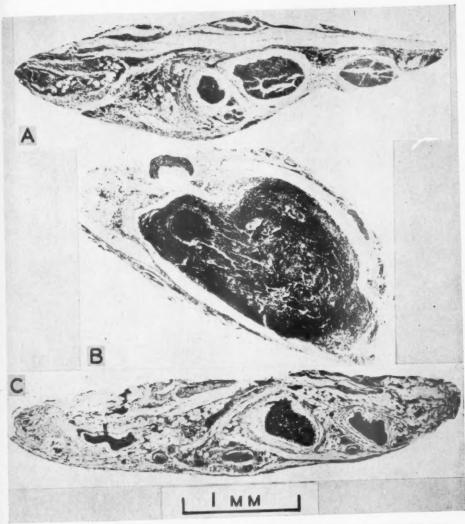
FIG. IV. Transverse sections of a multi-funiculated medial cutaneous nerve of the forearm twenty-one days after the insertion of plain catgut. Above (A), at (B) and below (C) the site of implantation. The photomicrographs illustrate the marked cellular reaction to the suture, the obliteration of funicular outlines by the reaction and the reappearance of the bundles at more distal levels.

of the foreign body and that when this function had been performed the reaction subsided leaving only a slightly denser connective tissue.

FIG. V. Transverse section of a musculo-cutaneous nerve one hundred and seventeen days after the insertion of plain gut. There is no trace of the marked cellular reaction which is such a characteristic feature of the sections at twenty-one days. There is a mild fibroblastic response and the reaction about the breached funiculus is little different from that observed in control specimens which suggests that needle trauma may have been responsible for some of the persistent fibrosis.

CHROMIC CATGUT.

Early changes at twenty-one days (Figs. VI, VII, VIII, IX):

The nerve was swollen at the site of implantation. The extent of this swelling varied from specimen to specimen, ranging from 2 to 10 times the original size of the nerve. The histological picture resembled that observed after the insertion of plain gut. There was a massive cellular reaction about the suture, which was disintegrating, with a very fine fibroblastic layer at the periphery. The predominant cell was the lymphocyte, and scattered among these were some polymorphs and histiocytes.

When the suture was confined to the epineurium the histological picture depended on whether the suture was tangentially placed (as in those specimens of the median and ulnar nerves in which the nerve was composed of a single major bundle with one or two small satellites) or whether it transfixed the nerve (as in nerves composed of a number of small bundles, e.g., the musculo-cutaneous nerve and the medial cutaneous nerve of the forearm). In the former the bundles were preserved but were displaced to the periphery of the mass

of cellular tissue which developed about the suture (Fig. VIII). This mass was larger than the funiculi and though well differentiated from the surrounding tissues there was little fibroblastic reaction so that only a fine indistinct peripheral capsule could be detected. The perineurium of the displaced bundles was only slightly thickened and internally the bundles showed no significant change. When the suture passed between the bundles, the great cellular response was responsible for the obliteration of the outlines of the bundles (Fig. IX). As a result the transverse sections prepared at the site of implantation showed a suture surrounded by a dense cellular mass in which no nerve tissue could be identified. Distally, however, the funicular outlines were restored.
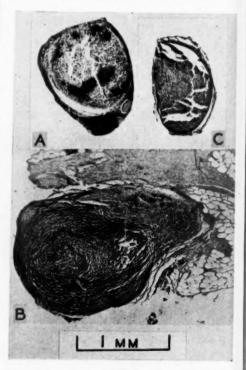

FIG. VI. Transverse sections of an ulner nerve twenty-one days after the insertion of chromic catgut. Above (A), at (B) and below (C) the site of implantation. The photomicrographs illustrate (i) the marked cellular reaction to the suture, (ii) the extension of this reaction proximally particularly as a perivascular cuffing, (iii) the obliteration of the funicular outline by the reaction, and (iv) the reappearance of the bundle at a lower level.
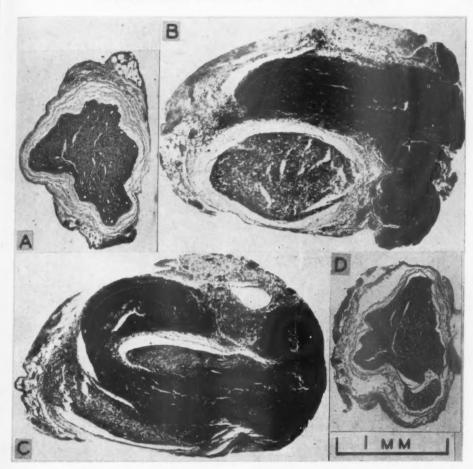
FIG. VII. Transverse sections of a median nerve twenty-one days after the insertion of chromic catgut. Above (A, B), at (C) and below (D) the site of implantation. Though the nerve has been transfixed and split into two divisions by the suture the marked cellular reaction is concentrated about the suture and has not spread to obliterate the outlines of the funiculus as in Fig. VI.

When the suture passed through a funiculus, the reaction varied from complete obliteration of the funiculus (Fig. VI), which occurred particularly when smaller bundles were involved, to a band of very cellular tissue which extended through the greatly thickened nerve about the margins of the suture (Fig. VII). The perineurium adjacent to the site of penetration was greatly thickened and in some preparations perineurial fibroblasts were observed migrating into the nerve bundle. The cellular reaction was sharply localised to the suture itself and was clearly demarcated from nerve fibres by a very fine indistinct fibroblastic capsule; the appearance suggested that the large funiculi had been split in two by the passage of the needle, the insertion of the gut and the subsequent reaction. The parts of the bundle not directly involved showed a mild cellular infiltration while the nerve fibres showed minimal interference, damage being confined to those directly involved by the passage of the needle.

Why the reaction should in one specimen obliterate the nerve and in another leave a clearly defined band running through it remains obscure.
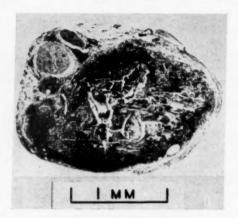
FIG. VIII. Transverse section of a medial cutaneous nerve of the forearm twenty-one days after the insertion of chromic catgut. The funiculi have been displaced to the periphery of the nerve by the mass of tissue developing about the suture.

Late changes at one hundred and seventeen days (Fig. X):

Only one specimen was available for analysis and this was of a through and through suture which passed between the funiculi. The nerve at the site of implantation was not swollen and no trace of the suture material could be found. The two small bundles composing the nerve were not damaged. However, in the region of implantation they showed some cellular infiltration, the perineurium was thickened and the epineurium was composed of denser connective tissue. The massive cellular reaction, which was such a feature in the early stages, was now represented by a mild permanent increase in the connective tissue elements.

The sequence of events in the extra- and intra-funicular tissues following implantation of this material was very similar to that observed after the implantation of plain catgut though the area of the surrounding reaction was about one half to twice as extensive. This is attributed, taking into consideration the slightly greater thickness of the chromic gut, to the chemicals used in its preparation.

HUMAN HAIR.

Early changes at twenty-one days (Figs. XI, XII, XIII):

The suture material was still present. The nerve was either not swollen at the site of implantation or showed a slight swelling which varied, depending on the specimen, from half to twice the original size of the nerve. The increase in size occurred when the nerve was composed of a single bundle while the dimensions were unaltered in multi-funiculated nerves where there was a larger amount of epineurial tissue to absorb the reaction.
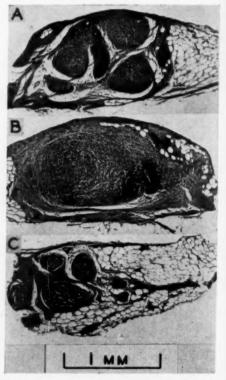

FIG. IX. Transverse sections of a medial cutaneous nerve of the forearm twenty-one days after the insertion of chromic catgut. Above (A), at (B) and below (C) the site of implantation. In this specimen the outlines of the funiculi were obliterated by the tissue developing about the suture but further distally the funiculi presented a normal appearance. Compare with Fig. VIII.

The area of reaction, which was sharply localised to the immediate vicinity of the suture, was composed predominantly of

fibroblasts and lymphocytes with t h e former slightly exceeding the latter though the reaction in each case was mild. The cellular response was very much less than that observed after the implantation of plain and chromic gut.
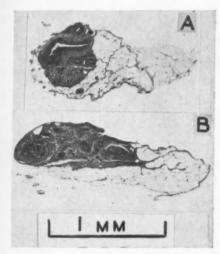

FIG. X. Transverse sections of a lateral cutaneous nerve of the forearm one hundred and seventeen days after the insertion of chromic gut. Above (A) and at (B) the site of implantation. There is no trace of the marked cellular reaction which was such a characteristic feature at twenty-one days. This has been replaced by a permanent fibrosis.

When the suture was confined to the epineurium it was surrounded by a narrow cellular zone which was in turn encircled by a well defined fibroblastic layer. The outlines of neighbouring bundles were preserved but the perineurium of these was slightly thickened though it was sharply demarcated from the subjacent nerve fibres.

When a funiculus was involved the outer limiting fibroblastic zone became continuous at the site of breaching with the neighbouring perineurium, which was slightly thickened. The contents of the bundle remained sharply differentiated from the encapsulated mass to which endoneurial and perineurial fibroblasts had contributed while the neighbouring parts of the bundle were mildly infiltrated with cells. In some specimens, however, the reaction was more severe. The perineurial thickening was greater and, in addition, perineurial fibroblasts had migrated into the involved bundle though

the intra-funicular migration was confined to the area adjacent to the suture. Despite the fact that the suture was well encapsulated that half of the bundle in which it reposed showed a much more intense cellular reaction (Fig. XI).

FIG. XI. Transverse section of a median nerve twenty-one days after the insertion of human hair which involved the funiculus tangentially. Though there is a mild reaction about the suture material the perineurium has been disorganised and fibroblasts are seen migrating into the bundle.

When small bundles were penetrated the reaction was always more severe, the involved area being converted into a tangled mass of nerve fibres, cells and fibroblasts— the reaction was mostly cellular (Figs. XII and XIII). This resulted in the complete loss of definition of the funiculus which could no longer be recognised. A short distance below the site of implantation, however, the involved bundles reformed and showed few signs of the gross involvement observed at more proximal levels.
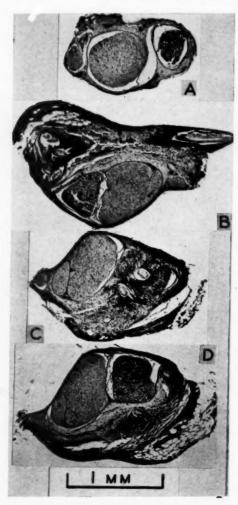
FIG. XII. Transverse sections of an ulnar nerve above (A) and at (B, C, D) the site of insertion of human hair which had been implanted twenty-one days previously. The extent and nature of the reaction to this material are illustrated together with the disorganisation of a funiculus following transfixation by the needle and suture. The involved bundle is again visible in the most distal section but carries traces of the injury at a higher level.

the changes in the involved bundles were usually of a minor character while the epineurial reaction was always insignificant.

FIG. XIII. Transverse sections of a medial cutaneous nerve of the forearm above (A), at (B) and below (C) the site of insertion of human hair which had been implanted twenty-one days previously. The series illustrates the nature and extent of the reaction in a multifuniculated nerve and the disorganisation of a funiculus following transfixation by the needle and suture. The involved bundle is again visible in the distal section but the entire nerve shows traces of the severe reaction obtaining at higher levels.

In general there was little reaction to human hair and in the early stages fibroblastic activity exceeded cellular so that at twenty-one days the implanted suture was definitely encapsulated. The reaction was confined to the immediate vicinity of the suture so that the involved area was of modest proportions. Because of the confined nature of the activity about the suture

Late changes at one hundred and seventeen days (Fig. XIV):

The suture material was still present and was encapsulated in fibrous tissue. The amount of swelling at the site of implantation appeared again to be related to the structure of the nerve. Thus an enlargement of three times was observed when the nerve was composed of a single funiculus but when there was sufficient epineurium to

absorb the reaction, as in the multi-funiculated variety, no enlargement could be detected.

FIG. XIV. Transverse sections of a multi-funiculated nerve (A and B) and one composed of a single bundle (C and D) one hundred and seventeen days after the insertion of human hair. The extent of the residual fibroblastic reaction is shown. Sections A and C were taken above the site of involvement and are included for purposes of comparison.

The epineurium was composed of dense connective tissue in the immediate vicinity of the suture and the perineurium of the involved bundles, though clearly demarcated from the nerve fibres, was grossly thickened. Where a large bundle had been breached, fibres had escaped externally and become entangled in the mass of tissue developing outside the perineurium. There was a localised cellular and fibroblastic reaction about the suture inside the bundle, the latter elements predominating to form a capsule about the retained suture material. The reaction had obviously shown no tendency to subside with the passage of time and the final picture suggested that, though the changes remained localised and were not invasive, there had been a continuous but slow increase in the fibroblastic reaction.

WHITE SILK.

Early changes at twenty-one days (Figs. XV and XVI):

The nerve was swollen at the site of implantation. The extent of this swelling varied from specimen to specimen, ranging from 4 to 13 times the original size of the nerve. The variation in the extent of the enlargement was not related to the size or structure of the nerve and appeared to be an individual characteristic.

The suture material was still present but was infiltrated with lymphocytes and polymorphonuclear leucocytes. The characteristic histological picture presented by the involved segment of the nerve was an extensive area immediately surrounding the suture which was tightly packed with cells and was well vascularised. In this cellular mass lymphocytes predominated but histiocytes and polymorphonuclear leucocytes participated in the reaction and there was a perivascular cuffing of plasma cells. Surrounding this cellular zone was a fibrous capsule which, though fine, was thicker than that observed after the insertion of plain and chromic gut and human hair.

When the suture was inserted tangentially through the epineurium, the encapsulated suture mass formed a lateral swelling which displaced but did not encroach upon the funiculi comprising the nerve. The epineurium surrounding the material was

thickened and provided the capsule for the cellular zone enveloping the suture. Only those bundles immediately adjacent to the suture showed signs of involvement. This consisted of some swelling and perineurial thickening together with a mild intra-funicular fibroblastic and cellular response which, in the case of small bundles, was generalised but which, in the larger bundles, was confined to those quadrant opposed to the suture.

When the suture passed between the component bundles those adjacent to the suture were submerged by the resulting intense cellular reaction and their outlines could no longer be identified. Transverse sections from the nerve below the site of implantation revealed, however, that, on emerging from the involved area, the normal funicular appearance was restored, the bundles showing few traces of the reaction which had obliterated them at a slightly higher level.

The effect of a transfixing suture on an involved bundle was influenced by such factors as the size of the latter and the manner in which the suture had been passed through it. The outlines of the smaller bundles, and occasionally those of the large
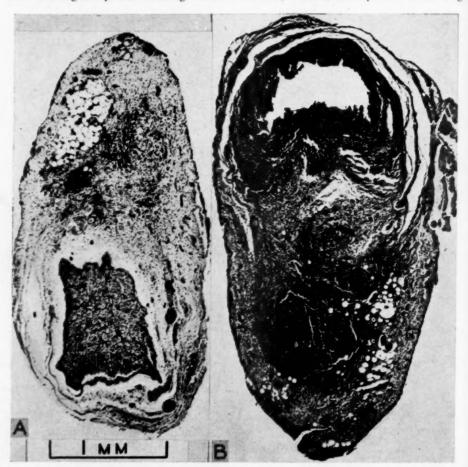

FIG. XV. Transverse sections of an ulnar nerve above (A) and at (B) the site of implantation of white silk which had been inserted twenty-one days previously. The massive cellular reaction which surrounds the suture and spreads to envelope and obliterate the funiculus is illustrated.

ones when they were not tangentially involved, were obliterated by the intense cellular reaction which developed though the funiculi reappeared at more distal levels. When, however, the involved bundle was the single or major funiculus of a large nerve (e.g., the ulnar or median), the general outlines of such large bundles were preserved though there was considerable distortion of their normal architecture in the vicinity of the implantation. In those specimens in which the perineurium had been tangentially ruptured, nerve fibres had herniated through the gap in the thickened perineurium and had become incorporated in the encapsulated fibro-cellular mass of tissue which had developed external to the funiculus. The direction of the reaction in these cases was away from the funiculus within which there was only a mild scattered fibroblastic and cellular response.

When, however, the suture traversed the central portion of the bundle or involved a large segment of it the surrounding zone was converted into a confused, tangled mass of cells, fibroblasts and nerve fibres. The perineurium could not be identified at the site of penetration while just beyond this point it was greatly thickened. Inside the funiculus, however, the reaction was concentrated about the suture so that those parts of the bundle not directly occupied by the suture and involved in the surrounding reaction retained their essential morphological features and showed only a mild cellular infiltration and fibroblastic response.

Despite the increased severity of the reaction which followed funicular penetration and which resulted in the disappearance of the characteristic architectural features of large numbers of nerve fibres, those submerged fibres which had not been herniated through the perineurium when this was breached and which had survived the actual passage of the needle and the initial trauma occasioned by the implantation of the suture appeared to have been preserved.

Late changes at one hundred and seventeen days (Figs. XVII and XVIII):

The suture material was retained and the involved segment of each nerve was enlarged approximately 4 times. Though the retained suture was enveloped in cells the essential

reaction was now fibroblastic in character and the mass was limited externally by a definite capsule.
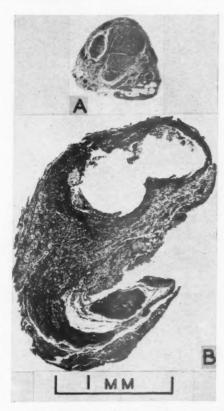
FIG. XVI. Transverse sections of a musculo-cutaneous nerve twenty-one days after the insertion of white silk. One funiculus has been breached and fibroblasts and nerve fibres are shown streaming away from the funiculus into the cellular tissue enveloping the suture. A section of the nerve above the site of implantation is included (A) for purposes of comparison.

There was a marked and extensive reaction in the epineurium about the retained suture material in which the fibroblasts greatly outnumbered the other cells and the surrounding connective tissue was much denser. This reaction was so extensive that, when the suture passed between funiculi, the latter were surrounded and their outlines were completely obliterated. The funicular pattern, however, was again restored further distally and the fibre damage appeared to have been minimal (Fig. XVII).
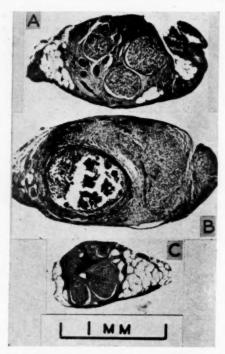
FIG. XVII. Transverse sections of a medial cutaneous nerve of the forearm above (A), at (B) and below (C) the site of implantation of white silk which had been inserted one hundred and seventeen days previously. The nature and extent of the reaction are illustrated together with the complete obliteration of the funicular pattern which has occurred at the site of implantation.

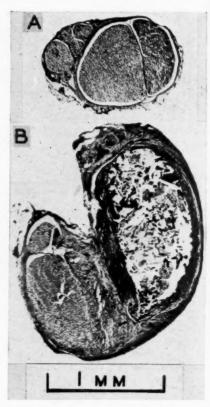
FIG. XVIII. Transverse sections of a median nerve one hundred and seventeen days after the insertion of white silk which has involved the funiculus tangentially. The reaction, which is much less in extent than at twenty-one days, is concentrated about the suture and only that section of the funiculus carrying the suture has been seriously affected. A section of the nerve above the site of implantation is included (A) for purposes of comparison.

Following tangential breaching of a large bundle the reaction was confined to the immediate vicinity of the suture material and as a result only that sector of the nerve containing the suture showed significant changes (Fig. XVIII). When the suture was more centrally placed the intra-funicular changes were more pronounced and exceeded those observed at twenty-one days. The suture material was now surrounded by a dense and thick mass of fibrous tissue while the neighbouring region of the bundle showed a mild cellular infiltration. Despite the extensive peri-sutural reaction in the transfixed bundles the damage to individual nerve fibres was far less than the histological picture suggested would be the case. Fibre injury appeared again to be confined to those fibres damaged during the implantation of the suture.

An analysis of the histological picture of the reaction to silk demonstrates, in particular, that: (i) the suture material was retained for one hundred and seventeen days; (ii) implantation of the suture excited a considerable reaction which was both cellular and fibroblastic, the former predominating in the early stages and the latter in the later stages; (iii) though the reaction tended to be self-limiting, the consequences were more serious when the perineurium and the interior of the funiculus were involved; and (iv) despite the considerable reaction, leading in some instances to the obliteration of the funicular pattern, involvement of nerve

fibres appeared to be minimal and to be confined to those originally damaged when the suture was being inserted. The fibre loss, however, was greater after one hundred and seventeen days than after twenty-one. No doubt the fibrosis which developed about the retained suture in the later stages would be responsible for deflecting regenerating axons from pathways which favour the restoration of original end-organ connexions.

TANTALUM.

Early changes at twenty-one days (Fig. XIX A, B, C, D, E):

The nerve was only slightly thickened at the site of implantation, the increase being from one-fifth to one-half the original size depending on the specimen; in one specimen, however, the nerve was enlarged to four times its original size. The characteris-
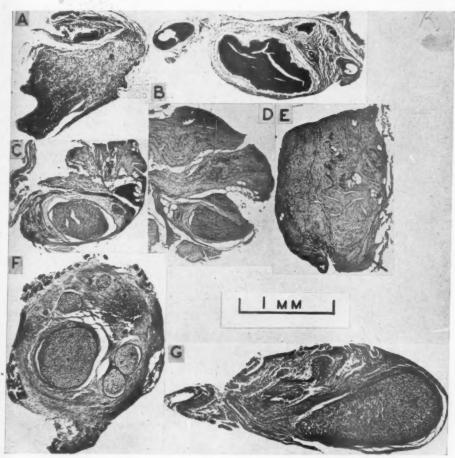
FIG. XIX. Transverse sections of several nerves to illustrate the reaction to the implantation of tantalum.

(A and B). Twenty-one days after implantation. The extent and nature of the reaction are shown. The reaction is concentrated about the suture and has not spread to involve or disorganise the nerve.

(C, D and E). Twenty-one days after implantation. In this specimen the funicular outlines of the nerve have been obliterated by a severe and extensive fibroblastic response. The arrow in section E is directed towards the site of the obliterated funiculus.

(F and G). One hundred and seventeen days after implantation. The sections illustrate the extensive residual fibrosis which results from the insertion of tantalum. Despite the severity of the fibrosis the funicular outlines of the bundles are retained unless the bundles have been transfixed.

tic feature of the histological picture in most specimens was the minor nature of the cellular and fibroblastic response.

When the suture was confined to the epineurium it was surrounded by a mild to medium cellular reaction in which lymphocytes predominated; beyond this there was a fibroblastic response which varied in intensity from specimen to specimen — mild in some, severe in others. The variation in the extent of the reaction appeared to be an individual peculiarity. Despite the variation in the intensity of the connective tissue reaction the perineurium of the adjacent bundles was usually unchanged while the cellular reaction observed inside the funiculi did not exceed the limits established by the investigation of control specimens. In one specimen, however, the funiculi comprising the nerve were obliterated by a particularly intense fibroblastic response (Figs. XIX C, D, E).

When the suture traversed a bundle the results depended on the size of the involved bundle. In the case of small bundles the cellular reaction, though localised, was nevertheless sufficient to obliterate the outlines of the funiculus. When a large bundle was involved the reaction was again sharply localised so that it was confined to the section of the funiculus carrying the suture. There was a mild cellular response about the suture with an outer limiting fibroblastic zone which, at twenty-one days, had so encapsulated the suture that the mass was clearly demarcated from the intra-funicular contents. Elsewhere the bundle was only lightly infiltrated with cells. The destruction of nerve fibres was limited to those damaged during the passage of the needle and suture material.

Late changes at one hundred and seventeen days (Fig. XIX F and G):

The picture at one hundred and seventeen days was quite different from that seen at twenty-one days. The nerve at the site of implantation was now swollen from 4 to 7 times its original size depending on the specimen. This was due to a very marked fibroblastic reaction which had spread diffusely through the entire nerve so that the picture was one in which the epineurium had increased considerably in amount and was composed of a much denser connective tissue with few blood vessels. Only a thin line of cells marked the track of the suture which had been gently removed prior to the preparation of the histological sections.

There was no invasion of the bundles not directly involved by the suture so that the funicular pattern was fully retained while the perineurium was only slightly thickened except where the suture material touched it and then it was greatly thickened. There was no cellular infiltration inside the bundles but the endoneurium of the individual fibres was thickened and was far more conspicuous than in any other specimens. When the bundles were traversed by the suture the fibroblastic reaction disorganised their contents and large numbers of nerve fibres were adversely affected.

NYLON.

Early changes at twenty-one days (Figs. XX and XXI):

The nerves were greatly swollen at the site of implantation. The median and ulnar nerves were enlarged approximately 6 times but the medial cutaneous nerve of the forearm and the musculocutaneous nerve were enlarged 18 and 16 times their original size respectively. The characteristic feature of the reaction was the tremendous fibroblastic response which was separated from the suture by a very thin cellular zone composed of lymphocytes and an occasional polymorphonuclear leucocyte.

The extensive fibroblastic reaction in the epineurium spread widely to surround, and sometimes submerge, the small funiculi. The larger bundles, however, were resistant to this epineurial reaction so that their essential outlines were preserved, though the perineurium was thickened wherever the fibroblastic mass established contact with it and inside the bundles there was a diffuse cellular infiltration which was maximal, but slight, at the site of the perineurial thickening. Even when the suture involved the perineurium of large bundles there was no or

very little fibroblastic invasion of the bundle. On the contrary, nerve fibres herniated externally to mingle with the fibroblastic mass which developed outside the bundle. The resistance of the large bundles to the encroachment of the fibroblastic reaction was a noticeable feature of the preparations.

of the intraneural architecture which occurred at the site of implantation, the nerve trunk was reconstituted distally and there presented a structure which was not greatly different from the normal. Apparently the only fibres damaged were those traumatised by the needle and suture; the others, though
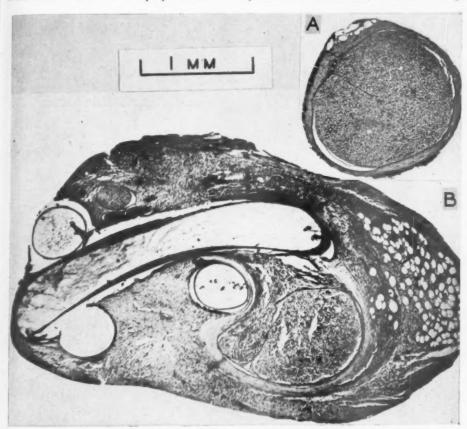
FIG. XX. Transverse sections of a median nerve twenty-one days after the insertion of nylon which has just clipped the major funiculus. The fibroblastic response predominates but the essential outlines of the bundles have been preserved. A section of the nerve above the site of implantation has been included (A) for purposes of comparison and to illustrate the perineurial thickening which extends proximally.

When the bundles were transfixed by the suture the fibroblastic response again dominated the picture but in addition the cellular reaction was greater in degree than when the suture was confined to the epineurium. In these cases funicular outlines were completly obliterated and all traces of individual nerve fibres were lost in the fibrocellular mass. Despite the complete disorganisation

dispersed and intermingled with the proliferating fibroblastic and cellular tissues, presumably continued unharmed through the zone of reaction.

Late changes at one hundred and seventeen days (Fig. XXII):

No trace of the suture could be found in the nerve. At the site of implantation the
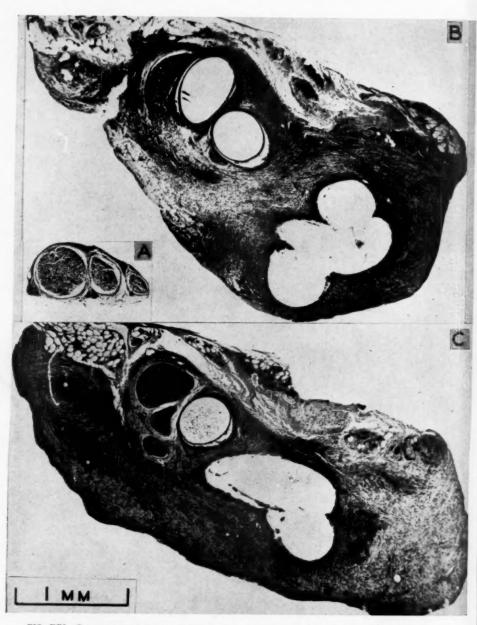
FIG. XXI. Transverse sections of a medial cutaneous nerve of the forearm above (A) and at (B and C) the site of implantation of nylon which had been inserted twenty-one days previously. The tremendous fibroblastic reaction is clearly shown. Despite the disorganisation of the funicular pattern shown in B, the bundles are again clearly defined in C which is at a more distal level.

nerve was swollen to 12 times its original size and was composed of a mass of dense fibroblastic tissue. Proximally, bundles which were normal in appearance entered and were lost in this mass but they emerged from it below. Despite the loss of funicular outlines in the fibrotic mass, collections of nerve fibres could still be identified. The histological picture indicated that perineurial fibroblasts had participated in the reaction and had blended with those originating external to the bundles.

FIG. XXII. Transverse sections of a musculo-cutaneous nerve to illustrate the extensive residual fibrosis which is evident one hundred and seventeen days after the insertion of nylon. A section from the nerve above the site of implantation is included (A) for purposes of comparison.

THE REACTION TO THE IMPLANTATION OF SUTURE MATERIALS.

GENERAL CONSIDERATIONS.

The following features were common to all the suture materials investigated.

1. A reaction is inevitable when suture materials are implanted in a nerve.

2. Though the centre of maximal activity was the suture material the reaction extended considerable distances up and down the nerve. The proximo-distal extent of the cellular response ex-

ceeded that of the fibroblastic, and was essentially perivascular in its distribution, while in each case the proximal spread was usually the more extensive.

3. The degree of the reaction was related to the surface area presented by the suture. Thus finer sutures produce relatively less reaction than the heavier while a greater reaction results when greater lengths are buried in the nerve.

4. The essential features of the reaction were a cellular infiltration concentrated about the surface of the suture and enveloping this a fibroblastic response from which a capsule for the entire mass was elaborated. The extent of the reaction and the degree to which the various elements (cells and fibroblasts) contributed varied with the particular suture used. In general a cellular response predominated in the case of absorbable sutures and a fibroblastic response when the non-absorbable variety was employed. It has already been noted that the extent of the reaction was influenced by the dimensions of the suture.

5. The suture and the mass of tissue which developed about it caused an enlargement of the nerve at the site of implantation in most specimens. In some specimens in which the nerve was composed of several small bundles with a large amount of inter-funicular tissue, the epineurial tissue absorbed the reaction so that the nerve was not enlarged.

6. In general, bundles which were not pierced and occupied by the suture resisted invasion by the mass of cells and fibroblasts which developed about it so that their outlines were preserved even though they came to be completely surrounded by the reaction. Occasionally, particularly following the insertion of tantalum and nylon, the perineurial surface opposed to the suture was thickened and the subjacent portion of the bundles showed a very mild cellular reaction so that there was no

clear line of definition between the perineurium and nerve fibres. In some specimens, however, the reaction was so intense and the adjacent bundles so small that the latter became submerged in the cellular mass in which they could not be identified.

7. When small funiculi were transfixed by the suture the reaction was usually sufficiently extensive to result in the obliteration of the outlines of the bundles. When, however, large bundles were involved in this way the reaction, which remained concentrated about the suture, was confined to the involved segment of the nerve and the more remote portions of the bundle showed no significant change. In some specimens the suture and associated reaction plugged the gap created in the perineurium so that no fibres escaped but usually nerve fibres herniated through the break and mingled with the tissue developing about the suture external to the funiculus. The extra-funicular reaction was usually more intense and extensive than that developing within the funiculus.

8. Nerve fibres appeared to be resistant to the reaction. Though the funicular outlines were sometimes obliterated by the reaction and the nerve fibres so modified that they could no longer be identified by their characteristic morphological appearance, the normal morphology of both the bundles and their contained fibres was, in most cases, restored at levels distal to the site of implantation. Furthermore there was considerable evidence to suggest that the majority of the nerve fibres altered in this way survived to function efficiently. The only fibres undergoing Wallerian degeneration were those which had been directly traumatised by the needle and those which had herniated through gaps created in the perineurium. Thus, Wallerian degeneration was much less than was anticipated would be the case from the conditions obtaining at

the site of implantation while below this level there was also little Schwann cell activity. Furthermore the cross-sectional area of the bundles below the site of involvement was unchanged or only slightly reduced in comparison with that obtaining at proximal levels. Other experiments have shown (Sunderland and Bradley, 1950) that the funicular cross-sectional area of the distal stump of a severed nerve which has been denervated for one hundred and seventeen days atrophies to about 40 per cent. of its original value. Post-operatively the animals, which were allowed the full freedom of a large cage so that their normal activities were unrestricted, showed no disturbances of motor function which could be detected by careful observation. Moreover muscles in the field of supply of the involved nerves showed no wasting which would have been evident twenty-one and one hundred and seventeen days after the injury; histological examination of these muscles revealed no changes indicative of denervation atrophy. All these findings pointed to minimal damage to the conducting elements of those nerve fibres whose outlines had been effaced as they traversed the area of reaction. For these reasons an examination of the tissue at the site of implantation without an examination of the nerve at more distal levels may give misleading information about the state of the funiculi and nerve fibres at the site of involvement.

The hazards to repair introduced by the reaction lie not in the damage inflicted on nerve fibres but in the introduction of tissues which, after nerve severance and repair, would exert an adverse influence on the regenerating axons firstly by deflecting them from a course which would favour the restoration of useful connexions and, later, by constricting them in the fibrosis at the suture line which develops as the end result of fibroblastic activity.

DISCUSSION.

In general the reaction set up by the implantation of a suture material introduces two distinct elements which behave quite

differently in relation to the suture material. The first comprises polymorphonuclear leucocytes, lymphocytes, histiocytes, giant cells and, in the case of silk, plasma cells. The activity of the cells is directed at the removal of the implanted foreign body. This activity was maximal in the early stages and later subsided when the suture had been absorbed or securely sealed off by fibroblastic activity. This reaction appears to be maximal at the time when regenerating axons would be crossing the suture line. However, observations made during the investigation indicate that nerve fibres are not harmed by this cellular reaction which in turn suggests that regenerating axons likewise would not be harmed. The possibility remains that this conglomeration of cells may divert axons from their correct course and in this way contribute to and aggravate the erroneous cross-shunting of axons which is inevitable after nerve repair. The possibility of deflection of axons appears to be much less under these conditions, however, than when the matrix is composed predominantly of fibroblasts and the fibrillar products of their activity. The amount and nature of the cellular activity in the initial stages, which is designed to remove the suture, cannot be regarded as a reliable measure of the influence which this activity exerts on axonal regeneration. If, however, such a reaction does exert any influence at all on regeneration it is possible, since some suture material set up a greater cellular reaction than others, to classify them on the basis of the extent of the cellular reaction which they induce. The order, proceeding from the most favourable to the least favourable, would be: Tantalum, human hair, nylon, plain catgut, silk, and chromic catgut.

The second elements which appear in increased numbers about the implanted suture are the fibroblasts. The fibroblastic activity is directed to the sealing off of the foreign body and to forming the residual tissue after it has been removed by phagocytic activity. The extent of this fibroblastic response, which reaches maximal proportions during the late stages, was dependent on the particular suture employed and the time for which it was retained. The reaction was therefore much greater and more extensive after the use of non-absorbable than after the use of absorbable sutures.

The fibroblastic reaction and the deposition of fibrillar material which follows it adversely influence regeneration in both the early and the late stages of repair. In the early stages the fibroblasts and their fibrillar products may ensnare regenerating axons and divert them from their proper course. This is particularly likely to occur when the fibrils form a disorganised matrix rather than parallel guide lines which are appropriately aligned to assist the passage of axons distally. In the later stages the scar tissue elaborated from the early fibroblastic reaction may constrict the regenerated fibres traversing it and in this way adversely affect conduction in them (Weiss and Taylor, 1944). For these reasons every attempt should be made to avoid fibrosis at the suture line. To achieve this, suture materials should be selected which do not promote or which are associated with a minimal fibroblastic response. When the suture materials are analysed on this basis they may be arranged in the following order of priority: plain catgut, chromic catgut and silk, human hair, tantalum and lastly nylon.

For these reasons the measure of usefulness of a suture material is determined principally by the fibroblastic reaction which it excites and not by the phagocytic response which is a transitory and temporary phenomenon concerned with the removal of the suture. Once the latter is removed these cells depart but if the material is retained many remain and contribute to the fibrosis.

It is important to keep in mind that the suture itself, if across the pathway of advancing axons, will obstruct and deflect them. All sutures do this regardless of whether they are of the absorbable or non-absorbable variety because regenerating axons sprout distally before the absorbable variety has been removed by phagocytic activity.

In searching for the most suitable suture material the following qualities are decisive:—

i. The suture material should set up a minimal fibroblastic reaction. In the early stages this reaction embarrasses and disturbs the normal growth distally of regenerating axons and at a later date will constrict them and therefore disturb conduction in them.

ii. The duration of the reaction should be as short as possible. In this connexion the absorbable have a distinct advantage over the non-absorbable variety.

iii. The material should be available in the finest calibre consistent with technical efficiency and the appropriate tensile strength so that a minimum of trauma is required for its insertion, the surface area in contact with the neural tissues is reduced to a minimum and the tensile strength is ade uate to maintain the nerve ends in apposition.

The sutures which best fulfil these conditions are plain catgut, human hair and silk. It is difficult to decide which is the most suitable of these three. Each possesses qualities not shared by the others. When factors other than the reaction induced by the suture are taken into account, e.g., sterility, tensile strength and fineness of calibre and ease of application, silk appears to be slightly superior to the other two. However, the reaction it induces is more likely to complicate the growth and subsequent function of regenerating axons than the absorbable catgut.

The question of plasma clot suture was not considered in this investigation. Introduced by Young and Medawar in 1940 this technique has been the subject of further and more detailed investigations by Tarlov and his co-workers (1943, 1944, 1948). Autologous plasma clot suture apparently results in very little inflammatory or fibrotic reaction and it is claimed that it permits a more precise matching of the nerve ends so that regeneration across the suture line occurs in a more orderly fashion. Despite the fact that a comparative study of the relative merits of plasma clot and silk demonstrated no consistent or striking differences between the two, Tarlov inclines to the belief that it is more frequently possible to obtain superior results with the former technique than by the use of conventional epineurial thread sutures. However, he wisely concludes that "the outcome following nerve suture does not depend solely on the employment of a certain method of repair, but to a large degree on the way in which a particular technique is used." Lyons and Woodhall (1949) have reported a serious reaction to fibrin film about the suture line after failed repairs.

As has been pointed out by Tarlov and Benjamin (1943) and Seddon and Medawar (1942) plasma clot suture is contra-indicated when tension exists at the suture line since there is a definite risk of separation of the nerve ends. The same applies when the ends of large nerves are to be maintained in apposition. The employment of through and through tension sutures to overcome separation is not the answer to this problem for reasons already stated. Under these conditions the conventional epineurial thread suture still remains unchallenged. Autologous plasma clot suture, however, has decided advantages when small nerves are being repaired or cable grafts inserted.

The use of plain catgut appears to have fallen into disfavour as the result of Sargent and Greenfield's (1919) observations in which the magnitude of the early cellular response was believed to be a reliable guide to the intensity of the fibrosis which would ultimately obtain at the suture line. At a later date a further and more valid reason was advanced for discontinuing the use of catgut and for replacing it by silk, namely the difficulty of obtaining a consistently sterile product for surgical use. If doubt exists concerning the sterility of this material, and this paper is not concerned with this aspect of the subject, it would be wise to avoid using it since there is no place in nerve surgery for a suture which might harbour infection. In this connexion it is interesting that the only wound which became

infected in this series was one in which cat-gut was inserted through the nerve. Provid-ing, however, this disadvantage can be over-come successfully we can see no reason why fine catgut should not be employed for uniting severed nerves. The reaction which it excites and the changes in its tensile strength which may occur following implan-tation do not contraindicate its use and in these properties it compares favourably with silk and human hair.

The severity of the late reaction to tan-talum is a contra-indication to the use of this material at the suture line, more remotely from it in the form of tension sutures, or as a protective wrapping. The claims that it is inert in tissues (Spurling, 1943; Spurling and Woodhall, 1946) appear to be based on inadequate experimental studies and one predicts that time will show that the use of this material, and particularly the use of ensheathing cuffs, has been productive of adverse effects at the suture line. In the belief that tantalum is biologically inert Norcross and Bakody (1947) attributed the adverse effects developing at the suture site after the use of tantalum cuffs to fragmenta-tion of the foil. There is good reason, how-ever, for suspecting that a contributing factor is the reaction induced by the presence of the foil. Lyons and Woodhall (1949) have recently reported on the adverse effects introduced by the faulty and improper application of tantalum cuffs.

Both the early and the late reaction to nylon were so severe as to exclude the use of this material for repairing nerves. Alexander *et al.* (1948) have described a technique for bridging gaps in nerves in which nylon strands were used as guide lines for regenerating axons. Though they have reported favourable results from their preliminary studies more extensive experi-mental trials will be necessary to establish these claims. There is good reason for believing, on the basis of the findings pro-vided by the present investigation, that the intense fibrosis which develops about the nylon will adversely influence regeneration both in the initial stages and later when the axons which have crossed the gap become involved in the fibrosing mass.

PRINCIPLES TO BE APPLIED WHEN INSERTING SUTURES.

A consideration of the data provided by this investigation suggests certain principles which should govern the method of applica-tion of sutures in nerve surgery.

1. Attention is directed to the trauma in-duced by the passage of the needle in the process of suturing the nerve. In many of the control experiments this was sufficient to promote a fibroblastic reaction along the needle track which was, however, localised and not in-vasive but which persisted as a perma-nent linear scar. Small funiculi traversed by the needle were distorted or their outlines completely obliterated by the reaction. In the case of large bundles, breaching the bundle resulted in the herniation of the subjacent fibres through the defect created in the peri-neurium and these became involved in the extra-funicular connective tissue reaction to form a lateral swelling com-posed of a tangled mass of tissue. Nerve fibre injury, however, appeared to be confined to those fibres either directly damaged by the needle or in-volved in the herniation.

   In order to minimise needle trauma the needle should be the finest which is consistent with technical efficiency and the needle tracks should be confined to the epineurium and so placed in that tissue that they do not lead to fibrosis in the pathway of regenerating axons; in other words they should be radially placed and external to the funiculi and since the extent of the reaction is proportional to the surface of the track taken, the number of times the needle is passed through the nerve should be reduced to a minimum. Though the question of herniation of fibres does not arise in the repair of severed nerves, since the funiculi have already been severed, it is important to remember that involvement of the perineurium increases the fibroblastic activity. This in turn leads to the

deposition of tissue which is a potential obstacle to the regeneration of axons in the appropriate direction distally, and this increases the hazards of repair.

2. The function of the sutures is to hold the nerve ends lightly opposed until union has occurred. Miller (1921) has shown experimentally (dogs) that "epineurial sutures of fine catgut or silk play little if any part in the strength of the suture line after the second week." The smallest amount of material that will safely accomplish this result should be used.

All suture materials promote a re-action, the extent of which is influenced, *inter alia*, by the surface area of the suture material in contact with the nerve. To reduce the extent of this re-action the surface area of the suture material should therefore be kept to a minimum. This is achieved by using fine, interrupted sutures and by insert-ing only the number required to main-tain union. Sutures used unnecessarily serve no useful purpose and only in-crease the hazards of repair by increas-ing the obstacles to the downgrowth of axons.

3. The sutures should be so inserted that they, and the reaction they excite, are not interposed between the funiculi of the proximal and distal stumps and therefore in the track of the regenerat-ing axons. To prevent this the suture should involve only the periphery of the epineurium. A peripheral reaction also tends to confine the regenerating axons internally and thereby hinders them escaping laterally at the suture line.

4. The sutures should not be absorbed before union is secure. There is evi-dence that union is secure by the third week. All the absorbable suture materials tested in this enquiry persisted for this period.

5. The perineurium should be avoided because damage to it increases the fibroblastic response. Piercing the perineurium above the site of nerve severance also allows the herniation of fibres at the site of breaching and this still further complicates regeneration.

6. Through and through anchoring sutures are to be avoided since they increase the chances of injury to nerve fibres particularly when the funiculi are in-volved. For this reason the practice should be discontinued of fixing the nerve at some distance from the suture line to prevent separation at the latter when union is effected under tension.

7. The biopsy studies of suture lines which have been excised owing to failure of recovery should take into consideration the fact that some of the fibrosis in-volving the suture line is unquestion-ably attributable to the suture material used particularly when the non-absorb-able variety, such as tantalum, have been employed. For these reasons the unfavourable histological picture pre-sented at the suture line should not be wholly and uncritically attributed to inadequate preparation of the nerve ends at the time of repair or such other factors as the time, subsequent to the injury, when this was undertaken. Several factors contribute to scarring at the suture line and the type of suture material and the method of its appli-cation often reach significant propor-tions.

8. The only acceptable measure of the value of a particular suture material or technique is not the nature and extent of the reaction they excite at the suture line or the number of nerve fibres which ultimately appear in the distal segment but the degree to which restoration of function occurs in the reinnervated tissues. In this connexion it should be remembered that factors other than the type of suture material employed influence healing at the suture line while additional factors, some of which defy measurement, com-bine to influence the extent and quality of the recovery after a nerve repair.

It will therefore be extremely difficult to reach any definite conclusion concerning the relative merits of different suture materials solely on the basis of end result analyses. For these reasons experimental investigations are of value only in so far as they assist in establishing certain general principles the application of which is likely to aid recovery and in revealing defects which adversely affect regenerative processes and should therefore be avoided. No more than this can be claimed for them.

SUMMARY.

1. The results have been described of an experimental investigation undertaken to determine the relative merits of a number of different suture materials for the repair of severed nerves.

2. Fine plain catgut, white silk and human hair are the most suitable materials for repairing nerves. Of these three silk has a slight advantage over plain catgut when technical factors as well as those associated with the reaction induced by the suture material are taken into consideration.

3. The outcome following nerve suture does not depend solely on the type of suture material employed but to a large degree on the manner in which it is used to unite the nerve ends. The principles which should govern the method of application of sutures in peripheral nerve surgery have been detailed.

TABLE 1.

Suture materials and nerves investigated.

Suture Material			Duration of experiment in days	Nerve					
Type	Diameter in inches	Preparation		Median	Ulnar	Medial cutaneous of forearm	Lateral cutaneous of forearm	Musculo-cutaneous of leg	Total
Plain Gut .. (00000)	·006	As obtained from the ampoule; rapidly passed through normal saline before use.	21 117	1	1	1	 1	2* 1	5 2
Chromic Gut (000)	·010	As obtained from the ampoule; rapidly passed through normal saline before use.	21 117	1	2	2	 1		5 1
Human Hair (Brunette)†	·005	Boiled for 30 minutes.	21 117	2 1	1	1 1		1	5 2
Tantalum ..	·005	Boiled for 30 minutes.	21 117	1	1 2	1		2	5 2
White Silk (000)	·010	Boiled for 30 minutes.	21 117	1 1	1	1 1		2	5 2
Nylon ..	·016	Boiled for 30 minutes.	21 117	1	1	1		1 1	4 1

† No chemicals had been used on the hair preceding removal.
* The wound became infected and the suture was discharged in one experiment.

TABLE 2.

Data relating to the extent of the reaction produced by the suture materials investigated.

Suture material and specimen	Nerve	Number of component funiculi *	Reaction after 21 days		Reaction after 117 days		Longitudinal extension of the reaction in mm.		Enlargement of the nerve trunk at site of implantation	Planimeter readings of the cross-sectional area of the nerve occupied by the reaction and the suture material except in the case of nylon and tantalum where the area occupied by the suture has been excluded. In sq. ins. at a magnification of 25.
							Proximal	Distal		
Plain Gut 2	M.	S	C4	F1			>27	21	4 x	1·14
2	U.	S	C4	F1			19	10	3 x	·80
2	MCF.	M	C4	F1			> 8	13	2 x	1·06
2	MC.	M	C4	F1			>22	20	6 x	·70
3	MC.	M								
10 S	LCF.	M			C1	F3	>17	> 4	2 x	·29
11 S	MC.	M			C1	F3	>14	5	0·3 x	·12
Chromic Gut										
3	M.	S	C4–5	F2			>19	26	4 x	2·10
3	U.	S	C4–5	F2			17	35	6 x	2·17
3	MCF.	M	C4–5	F1			>37	30	10 x	1·60
6	U.	S	C4–5	F2			18	34	9 x	2·0
6	MCF.	M	C4–5	F2–3			23	19	2 x	1·00
11 S	LCF.	M			C1	F3	> 2	8	No enlargement	·17
Human Hair										
5	M.	S	C2	F2–3			15	15	0·5 x	·15
5	U.	S	C3	F2–3			22	22	2 x	·36
6	M.	M	C2–3	F2			5	3	0·3 x	·35
5	MCF.	M	C3	F3			22	14	No enlargement	·37
10 S	M.	S			C1	F2–3	29	13	3 x	·40
11 S	MCF.	M			C1	F3–4	26	38	No enlargement	·20
Silk 1	M.	S	C4–5	F3			>22	> 5	4 x	·96
1	U.	S	C4–5	F3			15	>16	9 x	2·15
1	MCF.	M	C4–5	F3			11	8	4 x	> ·81
1	MC.	M	C4–5	F3			>11	>20	7 x	1·00
4	MC.	M	C4–5	F3			>23	15	13 x	2·10
10 S	MCF.	M			C3	F3	38	>26	4 x	·84
11 S	M.	S			C3	F3	38	38	4 x	·95
Tantalum 4	M.	S	C2	F2			8	3	0·5 x	·15
4	U.	S	C2	F2			14	17	0·5 x	·35
6	MC.	M	C2	F2–3			21	>20	2·3 x	1·00
5	MC.	M	C2	F2–3			>26	>26	4 x	1·8
4	MCF.	M	C2	F2			19	20	0·2 x	·04
10 S	U.	S			C1	F5	8	8	4 x	·80
11 S	U.	S			C1	F5	29	24	7 x	1·4
Nylon 7	M.	S	C2–3	F5			53	>30	6 x	2·70
7	U.	S	C2–3	F5			37	30	6 x	1·40
7	MC.	M	C2–3	F5			30	38	16 x	3·0
7	MCF.	M	C2–3	F5			>45	>26	18 x	1·40
10 S	MC.	M			C1	F5	>18	18	12 x	1·54

M—Median ; U—Ulnar ; MCF—Medial cutaneous of the forearm ; LCF—Lateral cutaneous of the forearm ; MC—Musculo-cutaneous of the leg.
* S—Single ; M—Multiple.

TABLE 3.

The relative suitability of the different suture materials arranged on the basis of the extent and the degree of the reaction which followed their insertion in the nerve.

Cellular reaction	Early fibroblastic reaction	Late fibroblastic reaction	Cross sectional area of the reaction at 21 days	Cross sectional area of the reaction at 117 days	Proximo-distal spread of the re-action
1. Tantalum	1. Plain gut	1. Plain gut	1. Human hair	1. Plain gut	1. Human hair
2. Human hair	2. Chromic gut	Chromic gut	Tantalum	Chromic gut	Tantalum
Nylon	3. Tantalum	Silk	2. Plain gut	2. Human hair	Plain gut
3. Plain gut	4. Human hair	2. Human hair	3. Silk	3. Silk	2. Silk
4. Silk	5. Silk	3. Tantalum	4. Chromic gut	4. Tantalum	Chromic gut
Chromic gut	6. Nylon	4. Nylon	5. Nylon	5. Nylon	3. Nylon

REFERENCES.

ALEXANDER, E., WOODS, R. P., and WEISS, P. (1948), *Proc. Soc. Exp. Biol. Med.*, vol. 68, page 380.

GUTTMANN, L. (1943), *Brit. J. Surg.*, vol. 30, page 370.

LYONS, W. R., and WOODHALL, B. (1949), "Atlas of Peripheral Nerve Injuries," London, W. B. Saunders Company.

MILLER, E. M. (1921), *Arch. Surg.*, vol. 2, page 167.

NORCROSS, N. C., and BAKODY, J. T. (1947), *J. Neurosurg.*, vol. 4, page 69.

PUDENZ, R. H. (1944), *Nav. med. Res. Inst. Project X-133.* Report No. 1, 19/2/1944, 13 pp. (not available in Australia).

SARGENT, P., and GREENFIELD, J. G. (1919), *Brit. Med. J.*, vol. 2, page 407.

SEDDON, H. J., and MEDAWAR, P. B. (1942), *Lancet*, vol. 2, page 87.

SPURLING, R. G. (1943), *Surg. Clin. N. Amer.*, vol. 23, page 1491.

SPURLING, R. G. (1944), *J. Neurosurg.*, vol. 1, page 133.

SPURLING, R. G., and WOODHALL, B. (1946), *Ann. Surg.*, vol. 123, page 731.

SUNDERLAND, S., and BRADLEY, K. C. (1950), *J. Comp. Neurol.* (in the press).

TARLOV, I. M., and BENJAMIN, B. (1943), *Surg. Gynec. Obstet.*, vol. 76, page 366.

TARLOV, I. M., DENSLOW, C., SWARZ, S., and PINELES, D. (1943), *Arch. Surg.*, vol. 47, page 44.

TARLOV, I. M. (1944), *Surgery*, vol. 15, page 257.

TARLOV, I. M. (1944), *J. Amer. Med. Assoc.*, vol. 126, page 741.

TARLOV, I. M., BOERNSTEIN, W., and BERMAN, D. (1948), *J. Neurosurg.*, vol. 5, page 62.

WEISS, P., and TAYLOR, A. C. (1944), *Proc. Soc. Exper. Biol. Med.*, vol. 55, page 77.

YOUNG, J. Z., and MEDAWAR, P. B. (1940), *Lancet*, vol. 2, page 126.

MALIGNANT DISEASE OF THE THYROID.

By Hugh R. G. Poate.

Sydney.

Introduction.

ON February 4, 1931, Sir Thomas Dunhill delivered the Arris and Gale Lecture on "Carcinoma of the Thyroid" and since then British surgeons have contributed but little to the study of this disease. In the United States of America a great deal has been written, particularly in the last ten years. The stimulus to the better understanding of the pathology of this lesion was given by Graham (1925) when he laid down the criteria of malignancy in thyroid tumours and evolved a working classification of such lesions thus bringing some order into the confusion that existed prior to that date.

As a direct result of his work many clinics have recorded their experiences over the past ten to twenty years and from 7 sources I have collected reports of surgically treated goitres totalling 20,102, among which were found 613 cases of carcinoma, i.e., 3 per cent. This figure is much the same as that given by Foss (1938) who averaged the reports of eleven authors giving an incidence of 2.37 per cent, and is comparable to that of Meissner and Lahey (1948) who, in a twenty year review of 19,000 operations for goitre, found that 439 of the glands removed were carcinomatous, or 2.3 per cent. When one excludes cases operated on for thyrotoxicosis, either the acute primary variety or that secondary to a colloid or nodular goitre, and for large simple colloid goitres, it leaves the nodular or adenomatous goitres which constitute 50 per cent. or more of these totals.

All authorities find that carcinoma simplex is a rare disease of the thyroid and that practically all cases of carcinoma of this gland arise in a pre-existing adenoma, so that the actual percentage of carcinoma in nodular or adenomatous goitre stands at about 5 per cent. of all such cases submitted to operation. My own experience is in accord with this figure but many authorities quote a much higher ratio, chiefly about the 7 per cent. mark (Cole, 1945; Hinton and Lord, 1945) though others referring only to the single nodule find some 15 per cent. malignant (Ramsay, 1948; Goldman, 1948). An intermediate figure comes from the Royal Free Hospital (London) where in eight years 530 nodular goitres were subjected to operation and of these 33, or 6.2 per cent. were carcinomatous (Branson and Houston, 1949). The most startling figures are those from the Mayo Clinic (Pemberton and Black, 1944), referring to goitre in children over a thirty-five year period, during which 53 children of fourteen years or under were operated upon and 18 of them, or 34 per cent., had a carcinomatous lesion. The youngest I have seen is a boy of four and a half years who is to be operated on shortly as he has a single, hard, irregular mass which has developed during the last three months. Ward *et al.* (1950), record a case of a boy of four years of age with a papillary growth invading the capsule.

It has been remarked (Kennedy, 1935), that "any palpable mass in the thyroid of a child should be suspected of possessing malignant qualities regardless of how innocent the mass might appear to be on clinical examination."

Some of the peculiarities of carcinoma of the thyroid as compared to carcinoma in general are that it knows no age limitation, size is no criterion of malignancy or otherwise, it most usually arises in a lesion apparently benign for most of a patient's lifetime (Case 1), and, in many cases, is compatible with a long period of life even with metastases in the lungs or bony skeleton although in other cases may cause death within a few months.

It will be noticed that the figures already quoted from the United States of America are for cases treated surgically and they have been subject to much criticism as to whether they are a true reflex of the incidence of thyroid carcinoma in the general population with goitre since those operated on have been well screened through the general practitioners, the out-patients departments of the

hospitals and even by the surgeons. Geo. Crile, Jr., in his recent book (1949) discusses this matter at some length and states "until we know more accurately how often benign adenomas become malignant it would seem wise to base indications for thyrodectomy on clinical judgment rather than on statistical surveys of selected or unfollowed cases."
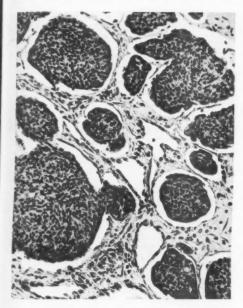

FIG. I.—Case 1. Mrs. H. H.: 60 years. Enlarged thyroid for thirty years but increasing on left side in last nine months. Diagnosed as malignant adenoma. 26th November, 1947. Left lobectomy. Carcinoma in large adenoma 7.2 x 5.2 cm. Marked invasion—could not classify. (x 100.)

It is a matter for regret that complete details have not been kept of one's personal experience but it is only in the last ten years or so that it has been possible to have routine examinations carried out on all specimens removed at operation. In a recent check made on 30 cases coming under notice in the last two years, either as new cases or old ones reporting for routine check, only 16 were considered fit for surgery and of these 5 were not diagnosed prior to operation. So far, only one young man, 20 years of age, whom I saw in consultation after operation for carcinoma simplex, died of metastases to the lungs two years later (Hoddle, 1949). Of those 14 cases considered inoperable and in whom there was no biopsy but who were regarded as clinically malignant, seven have

died within two years of diagnosis, despite repeated courses of irradiation, 3 have local masses in the neck but appear well and 4 seem to be quite clear of any trace of the disease, the longest survival being nine years. If this experience is general to most surgeons, then the disease must be more common than is generally thought and explains why the pathologists do not meet with many as in nearly every case they die in their own homes or in a private nursing home where facilities are not available for post-mortem examination. Pack and Livingstone (1940) quoted by Geo. Crile, Jr. (1949), remark "in the millions of non-toxic, symptomless and innocuous goitres which never are removed, the incidence of carcinoma is so low that vital statistics rate the thyroid sixteenth on the list of organs affected by malignant disease," and strangely enough the Government statistician of New South Wales does not list carcinoma in deaths from thyroid diseases in that State or did not do so up to 1947 (Gibson and Poate, 1949). It should be pointed out that in a great number of cases this disease is curable by adequate surgery followed by deep X-ray therapy so would not come within the purview of the statistician, or in many cases it has such a long life history that patients may die of some intercurrent disease and the thyroid malignancy is overlooked.

Carcinoma of the thyroid is seldom found in association with acute thyrotoxicosis, whether primary or secondary to a nodular goitre, and in the cases reported it would appear to have developed prior to or quite independent of the toxicity. Pemberton and Black (1948), in a collected series of 1,310 cases of carcinoma of the thyroid gland from 5 authors found 1.75 per cent. were associated with exophthalmic goitre. In 4 out of 10 of Pemberton's own cases the malignancy has developed in an adenoma, and other observers report similar incidence, but the fact remains that in some cases it does arise de novo. It is interesting to note that in many cases of carcinoma of the thyroid gland there may be some elevation of the basal metabolic rate and symptoms of a low-grade thyrotoxicosis which the patients have ignored. This probably results from hyperfunction due to hyperplasia in the benign gland tissue rather than in the malignant tissue.

In eleven years to 1946 at the Mayo Clinic in 3,500 operations for exophthalmic goitre 15 cases of carcinoma were found, i.e., 0.4 per cent. which had not originated in an adenoma.

FIG. II—Case 2. Mrs. A. M. L.: 48 years. 11th January, 1949. Enlarged thyroid since her teens—recent enlargement right side. Adenoma right lobe. 17th January, 1949. Right lobectomy. Carcinoma.

DIAGNOSIS.

Carcinoma of the thyroid is not as common as in stomach, breast, uterus, colon, etc., but does have a definite rate of occurrence. In advanced stages the condition of the patient is most distressing and everyone should be familiar with its possibility and means of prevention. By the time diagnosis is undoubted as evidenced by a hard, irregular, fixed mass often with metastases to cervical lymph glands, lungs, etc., or with altered voice from nerve involvement, adequate surgical treatment is impossible in most cases. Usually these patients have had an adenomatous goitre for a great number of years and have been told by their family physician that there is no need to worry about it (Case 2). All clinics report in similar terms and it is high time that the profession at large learned at least to warn

patients that if any change at all occurred in the goitre they should report forthwith for examination. The usual history is that the tumour has begun to increase in size over a period of months and has altered in consistency becoming hard and irregular. In such cases the onset of carcinoma should be suspected and operation advised as there are no reliable positive signs or symptoms of any value for assisting in early diagnosis.

Recent and progressive development of a single nodule, especially in middle life, should be regarded with suspicion. Sudden swelling in a pre-existing nodule of long standing with pain and tenderness suggesting haemorrhage into the tumour is likely to be of grave import especially in those over 50 years of age. A single mass in one lobe of the thyroid irrespective of the age of the patient is also to be regarded with suspicion, particularly in a male, as carcinoma is about twice as common as in a similar tumour in a female.

FIG. III.—Case 3. Mr. J. F. P.: 43 years. Large thyroid for years. Was in two hospitals nine or ten years ago but nothing was done. It has become hard and irregular and he has had bad cough in last six months. Appears to be malignant. 9th September, 1949. Carcinoma infiltrating trachea. Partial resection only. Lot of calcification. Papillary formation with unusually dense fibrous core but appearances vary. Carcinoma. For Deep X-ray. Was very well and apparently clear of any trouble, 3rd June, 1950. (x 100.)

Cattell (1946), is very emphatic that all discrete adenomata require operation irrespective of the age of the patient, and all authorities of experience are in entire agreement with this opinion. Lockwood (1947), regards this aspect so seriously that one Sunday morning when he had a little more time than usual to shave, noticing a nodule

in the
remove
work a

In th
the th
which
mistake
even h
gland.

(1.)
tioned
life, es

(2)
rence i
absence

FIG. IV
ber, 194
years.
11th No
adeno-ca

(3)
fusing
moto
lobe
whole
tumou
carcin
Hashi

in the right lobe of this thyroid, he had it removed on the Thursday and was back at work a week later.

In the differential diagnosis of lesions of the thyroid there are several conditions which have to be considered and may be mistaken clinically for carcinoma or may even be associated with carcinoma of this gland.

(1.) Haemorrhage has already been mentioned and is of some concern in middle life, especially in a single nodule;

(2) Calcification is of common occurrence in old adenomata but does not indicate absence of malignancy (Case 3);
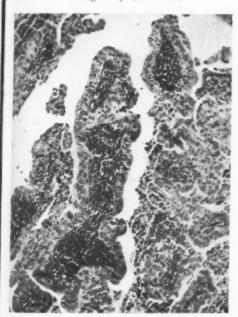

FIG. IV.—Case 4. Mrs. C. M. G.: 47 years. 4th November, 1949. Swelling right lobe of thyroid for three years. Hard irregular mass seems malignant clinically. 11th November, 1949. Total thyroidectomy. Papillary adeno-carcinoma in Hashimoto's disease, also has Hurthle cells present. (x 100.)

(3) Chronic thyroiditis is apt to be confusing whether it be of the Riedel or Hashimoto type, the former usually involves one lobe but the latter gradually involves the whole gland and the even hardness of the tumour differentiates these conditions from carcinoma. I have not seen any record of Hashimoto's disease being associated with

carcinoma but have recently met with two such cases (Case 4). Only one case is on record of carcinoma in a Riedel's struma (Dinsmore, 1948).
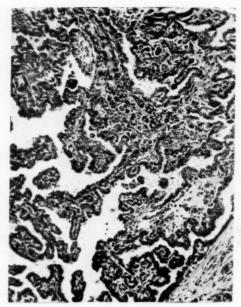
(4) Acute or sub-acute thyroiditis is usually associated with an even smooth enlargement of the gland which is very tender and there may be some elevation of temperature with accompanying general symptoms. These conditions yield magically to deep X-ray therapy. Abscess formation is very rare; I have seen only one case associated with carcinoma.

Aspiration biopsies have been advocated (Watson and Pool, 1940), and it is claimed that a positive diagnosis can be made in 80 per cent. of cases but where carcinoma is suspected it is a procedure one would hesitate to adopt for fear of spreading malignant cells in the surrounding tissues which probably may not yet be involved. Also as carcinoma usually occurs in one part of an adenoma it could easily be missed.

Frozen sections have proved unreliable (Lange and Maclean, 1949), as even with deliberate microscopical examination, several areas of the tumour may need close scrutiny before a positive diagnosis can be given even by a most experienced pathologist. If in doubt, the surgeon should regard the lesion as carcinoma and proceed with a radical operation as being in the best interests of his patient.

The only type of carcinoma which is readily recognisable is the papillary variety which occurs in relatively young people and is characterised by multiple metastases to the cervical lymph glands. These cases were considered for some years to be tumours in lateral aberrant thyroid tissue but it is now generally agreed that a primary focus can always be found in the thyroid. This variety is one where excision of an involved lymph gland is permissable to establish diagnosis.

Radioactive iodine can play a part in diagnosis as in normal gland tissue and in benign tumours the capacity to collect iodine is very evident but in carcinoma this unique function is completely lost in the majority of cases and in the balance it is enormously reduced (Rawson, 1947). Stress has been laid on the enlargement of the pre-laryngeal lymph gland (Delphian node) but I have not found it helpful in diagnosis.
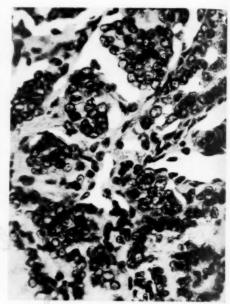
FIG. V. — Case 5. (x 100.)

FIG. VI. — Case 5. (x 200.)

Mrs. J. H.: 27 years. Seen 28th October, 1949. Has baby 2 years old and soon after the birth a swelling developed in upper pole right thyroid. Subsided greatly on taking thyroid substance but has a small, firm nodule present. Over the last ten months swellings have developed both sides of neck and in supraclavicular areas also. X-ray chest clear. 21st December, 1949. Right lobectomy and huge lymph gland under right sterno-mastoid was removed. Papillary carcinoma in both thyroid and lymph gland. 22nd February, 1950. Extensive resection of glands right side of neck. 1st March, 1950. Similar resection of glands left side of neck. All glands show papillary carcinoma corresponding to that in the thyroid.

Aetiological Factors.

The main factor determining carcinoma in the thyroid is the existence of a single adenomatous nodule and it is thought that the foetal adenoma is the most dangerous. For many years warnings have been given as to the use of iodine in cases of adenomatous or nodular goitre and Warthin's (1929) opinion is still held today as follows: "proliferation of the adenoma cells appears to result from over-iodinization. A peculiar hypertrophy of the adenoma is produced and transitional stages between such hypertrophic proliferating adenomas and carcinoma have been observed. It is an open question whether the over-use of iodine may not stimulate the development of carcinomatous transformation of an adenoma in a patient possessing also the cancer-susceptibility constitution."

Since the introduction of the "thio" compounds for the control of thyrotoxicosis, various writers have raised the question as to whether this form of therapy "may not fortify the cancer-susceptibility factors (as yet unknown) leading to a higher incidence of malignancy in the human thyroid." (Editorial, J. Amer. Med. Assoc., 1945.) It has been pointed out that the histology of glands removed at operation shortly after preparation with a "thio" derivative shows marked "hyperplasia with heightened epithelium, marked papillary infolding and mitoses in the epithelial cells." (Broders and Parkhill, 1944.)

Bielschowsky (1944), in Great Britain, working with the relatively newly discovered and unusually powerful carcinogen 2 acetoamino-fluorine found it produced carcinoma in various organs but not in the thyroid until it was fed to animals in which hyperplasia of this gland had been induced with thiourea when invasive epithelial tumours developed. Apparently antecedent or concurrent hyperplasia was a necessary and decisive factor in the production of these

thyroid tumours. "Thus a chemical that causes hyperplasia limited to a single organ prepared that organ for carcinogenesis by a chemical which normally is effective only on other tissues." (Editorial, J. Amer. Med. Assoc., 1945.) As against these facts two important points stand out. Firstly, no authenticated case of carcinoma arising in an acute primary toxic goitre treated with any "thio" compound has yet been reported nor have I seen any report of the onset of malignancy in a toxic adenoma so treated where the possibility of its development would be more likely. Secondly, in my own experience with long-term therapy the hyperplasia clears in 64 per cent. of cases, the gland reverts to normal and the patient is completely free of any signs or symptoms of their pre-existing thyrotoxicosis. Of the remaining 36 per cent of cases, in 2 per cent. the therapy was abandoned and 34 per cent. showed evidence of pre-existing but now controlled thyrotoxicosis, e.g., prominent eyes, nervous instability or a persistently enlarged gland, the latter in 15 per cent. of the cases. As recurrence of thyrotoxicosis was noted in several of these, they and all others were advised to undergo operation. The gland in those who had recurrence of symptoms showed areas of hyperplasia still present but in those who had no recurrence the gland was completely clear of any hyperplasia and was in a resting colloid stage (Poate, 1950).

If the advice again given is followed that all cases of toxic adenomatous or nodular thyroids should be submitted to operation and that all those acute primary cases where glandular hypertrophy persists and thyrotoxic symptoms recur should also be advised operation, there should be no fear that carcinoma will develop in the few unfortunates who may have a cancerous diathesis.

PROPHYLAXIS.

As will be gathered from remarks already made, a pre-existing adenomatous goitre, especially the single nodule, is the outstanding factor in the onset of carcinoma in the thyroid. Not only in the thyroid but in other organs it is well recognised that malignancy may supervene in some apparently benign condition after a variable and indefinite period of time. The early recognition and removal of such pre-cancerous lesions is the best prophylaxis for cancer and its control. Geo. Crile, Jr. (1949), very pertinently remarks: "The danger is not that a discrete adenoma may become malignant but that it is already malignant," to which one may add that malignancy may be developing nearby as exemplified by the following case.

A few months ago a woman of about thirty years presented with an adenoma in the left lobe of her thyroid of two years' duration and about the size of a walnut. This was excised widely but on routine examination of the right lobe a small area of hardness on the surface was noticed only about 0.5 cm. across. It was excised and proved to be adeno-carcinoma. This is the earliest case I have met with. The adenoma was simple (Case 6).

FIG. VII.—Case 6. Mrs. M. A.: 36 years. Adenoma left lobe of two months' duration only. 16th January, 1950. Resected adenoma. Found hard area on surface of right lobe which was resected. Adenoma was simple foetal type. Right lobe area was papillary adeno-carcinoma. (x 100.)

Hinton and Lord (1945), examined a series of 200 apparently benign solitary nodules removed from breasts and 184 removed from thyroids. In the breast series 6.7 per cent. showed carcinoma, whereas 7.6 per cent. of the thyroid nodules were malignant. I doubt whether any medical man would advise a patient with a tumour

in the breast to do otherwise than have it removed, yet such advice is the exception with thyroid nodules and it is generally the patient and not the doctor who raises the question of operation.
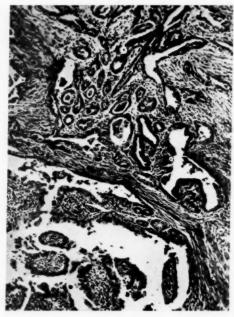

FIG. VIII.—Case 7. Miss E. D.: 48 years. Swelling in neck five years, but has enlarged in last year. 27th August, 1947. Subtotal thyroidectomy with adherent musculature, weight 65 g. Papillary adeno-carcinoma on one of multiple colloid adenomata. (x 100.)

In cases of multiple adenomatous goitres the position is very different as so many of these are late stage involutionary colloid adenomata developing on a simple colloid goitre dating back to adolescence. Such goitres do not call for operation except when (1) one area begins to enlarge and becomes hard or irregular (Cases 7 and 8), (2) pressure symptoms develop, (3) thyrotoxicosis supervenes or (4) for cosmetic reasons.

PATHOLOGY AND CLASSIFICATION.

In his classical article published in 1924, Graham, in referring to carcinoma of the thyroid arising in adenomata, stated "we find all grades of transition of the original adenoma into all types and combinations of morphological cancer mentioned in the literature except pure papilliferous adeno-carcinoma and pure schirrous carcinoma." He laid down the criterion for malignancy as being invasion by tumour cells of the lymph and blood vessels. The papilliferous carcinomata are invaders of the lymphatics and constitute 15 per cent. of all cases, whereas the balance of 85 per cent. represent the malignant adenomata which invade blood vessels, hence the difference in prognosis. It is not always possible to demonstrate vascular invasion so one must take into account invasion of the capsule, of adjacent thyroid tissue and nearby muscle or other structures.

FIG. IX.—Case 8. Mrs. L. M. B.: 40 years. Enlarged thyroid for seventeen years apparently multiple colloid adenomatous goitre. 12th December, 1949. Total thyroidectomy, weight 103 g., as one area suspicious. Papillary adeno-carcinoma on colloid adenoma. (x 100.)

Many and varied classifications have been presented and we can leave them to the pathologists for argument. The surgeon is more concerned in a simple and practical grouping such as suggested by Ward (1944), particularly as it is based on prognostic and therapeutic criteria.

Group I: Papillary carcinomata

Group II: Malignant adenomata

Group III: All others including schirrous, small-cell and large-cell types, undifferentiated carcinomata, etc.

The classification used by the American Goitre Association and now generally accepted is that suggested by Warren (1940) adopted from Graham (1924) as follows:

1. Low grade malignancy

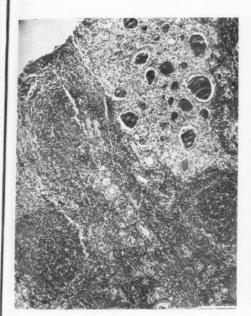(a) Adenoma with blood vessel invasion,

(b) Papillary cystadenoma.

(a) and (b) are frequently grouped together.

2. Moderate grade of malignancy
   (a) Papillary adenocarcinoma,
   (b) Alveolar adenocarcinoma,
   (c) Hurthle cell carcinoma.

3. High grade malignancy
   (a) Small cell or carcinoma simplex (compact and diffuse type),
   (b) Giant cell carcinoma,
   (c) Epidermoid carcinoma,
   (d) Fibrosarcoma,
   (e) Angiosarcoma.

Sarcoma of the thyroid does occur but most authorities consider it a rarity and that many cases classed as sarcoma are really highly anaplastic carcinomata. Pemberton (1939), in 774 malignant tumours of the thyroid found only 4 cases and I have seen only one undoubted case of the large spindle-cell type.
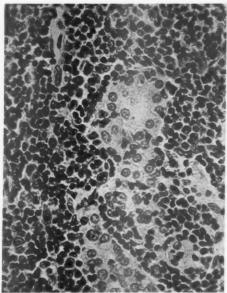

FIG. X. — Case 9. (x 100.)

FIG. XI — Case 9. (x 200.)

Mrs. L. W.: 54 years. 23rd March, 1945. Large adenoma left lobe noticed eighteen months. Operation advised but took thyroid tablets. 23rd July, 1947. Says lump cleared on left side but now has large mass in right lobe. 11th August, 1947. Total thyroidectomy for infiltrating tumour involving right inferior laryngeal nerve. 193 g. in weight. Deep X-ray therapy advised. Largely lymphoid. Some Hurthle cells. Capsule infiltrated. ? Lympho-blastoma; ? Lympho-sarcoma. Five weeks after operation had large mass in right side of neck. Cleared with X-ray. 6th March, 1950. Apparently normal but needs gr.ii dry thyroid extract twice daily.

There is considerable divergence of opinion regarding Hurthle cell tumours of the thyroid and most authorities class them as carcinoma of a moderate grade of malignancy.

FIG. XII. — Case 10. Mr. C. H. V.: 44 years. 5th October, 1944. Mass in neck twenty-five years with recent enlargement. Large adenoma left lobe. 23rd October, 1944. Left lobectomy. NOT examined as was thought simple. 18th October, 1948. Small nodule under centre of left sterno-mastoid. 12th April, 1950. Mass had enlarged considerably so extensive resection was performed. Papillary adeno-carcinoma. (x 100.)

The characteristic Hurthle cell is large, pale, clear, eosinophil staining, with a large nucleus (Case 9). It has been pointed out (Friedman, 1949), that their existence in tumours has been more widely recognised than their presence in non-neoplastic lesions of the thyroid. They have been met with in thyroid hyperplasia, Hashimoto's disease, myxoedema, exhaustion-atrophy and after irradiation or partial thyroidectomy and in these conditions may be regarded as a form of cellular involution in lesions of the thyroid of a regressive nature (Childs, 1950). However, there is no doubt that they do give rise to tumour formation (Case 11) but in the 18 cases I have met with over the last twelve years, malignancy, if any, must be of a very low grade. I consider there are two types—one occurring in young people under twenty years of age and the other in women over forty years. I have seen only one case of tumour formation of this variety in a male, who was twenty years of age when operated upon (Case 12). The most interesting case was in a girl of 12 years, who had two discrete nodules in the right lobe and one in the left lobe, each about 2.0 cm. in diameter, completely encapsuled and consisting wholly of Hurthle cells. They were removed by local excision some eight years ago and there has been no recurrence in this or any of my cases.
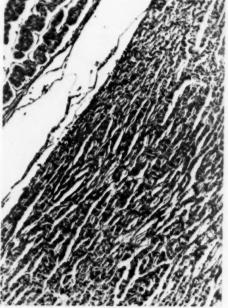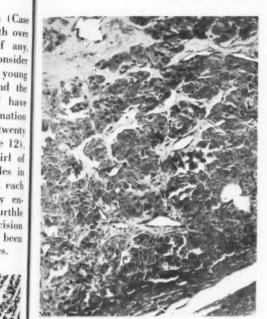

FIG. XIII.—Case 11. Mrs. A. A.: 51 years. Tumour present for some years gradually enlarging. This section is illustrative of the columnar form of Hurthle cell tumour. The usual arrangement is acinar. (x 100.)

Secondary metastases to the thyroid from malignant tumours elsewhere is very uncommon and I have seen only two cases — one from breast and one from kidney.
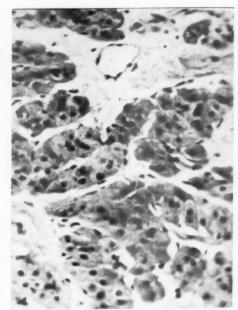
FIG. XIV. — Case 12. (x 100.)   FIG. XV. — Case 12. (x 200.)

Mr. R. T.: 20 years. 18th April, 1950. Has noticed gradual enlargement in thyroid area for two years. Irregular nodular medium-sized goitre clinically malignant but is mobile. 3rd May, 1950. Total Thyroidectomy performed. Pathologist reports Hurthle cell adenomata.

PROGNOSIS.

This depends very largely on the time of diagnosis and the type of lesion but as Ward (1944) has pointed out, one should speak of "survival" rather than "cure" rates owing to the extraordinary variegations of some thyroid tumours. This is well exemplified by the case of a male aged forty-nine years from whom I removed the right lobe of the thyroid in February, 1932. The pathologist reported adenocarcinoma. He was quite well until the end of 1947, when he noticed a lump low down in the right posterior triangle of the neck. A radical dissection was performed and the histological picture was identical with the original tumour. Many such cases are recorded in the literature.

The pure papillary growths of young people which used to be called "lateral aberrant thyroid tumours" have an excellent prognosis provided removal of all lymph glands is carried out along with a hemithyroidectomy on the side of the thyroid in which the primary tumour is located or if it cannot be found total thyroidectomy should be performed.

In the average case where diagnosis has been established following operation and the tumour is still encapsuled, the outlook is very favourable as lymph channels are very poor in adenomata and even though there be blood vessel invasion it is rare to see metastases until the capsule or surrounding gland tissue is involved. The late stage cases with fixity of the tumour generally have metastases in lung or bone and are usually dead within two years of diagnosis despite intensive deep X-ray therapy but now and again one seems to survive for a considerable period, the longest I have met with being nine years.

Many authorities consider irradiation useless in an angio-invasive tumour but I do not subscribe to this view and advise it in all cases as is done in the Lahey Clinic regardless of the pathological type or extent of involvement (Lahey, 1940; Meissner, 1948). The only exception I make is in the pure papillary tumours.

The longest duration I have known was in a woman who, at the age of fourteen, developed a tumour in the right lobe of her thyroid. Nothing

was done until 1917 when she was twenty-seven years of age. Further operations were carried out in 1922 and 1928 but unfortunately no records are available. I first saw her in December, 1930, when she had a supra-sternal mass and one on the left side of the neck, which were removed in January, 1931, and proved to be adeno-carcinoma. Deep X-ray was given and again repeated in November, 1933 as a mass had developed above the sternal notch. She remained well until December, 1943, when a small nodule became evident below the medial end of the left clavicle but, being extremely tender, was thought to be a neuroma. This increased very slowly and, in April, 1947, it was excised under local analgesia, being then about 1.5 cm. in diameter and proved to consist mainly of Hurthle cells. A firm mass had developed above the sternum and the trachea was fixed but it seemed more like a fibrosis than recurrence. In October, 1949, she complained of increasing difficulty in breathing which gradually became worse, so, in March, 1950, a bronchoscopy was performed. The trachea was very constricted for some 5.0 cm. and there was a small papilloma in its lumen which appeared to be the cause of her dyspnoea. This was removed with immediate relief and proved to be carcinomatous but could not be classified. She is now sixty years of age and should be able to carry on for some years more.

TREATMENT.

Enucleation of an adenoma of the thyroid is an unwise procedure and it should be excised with some of the surrounding gland tissue if of moderate size but removal of the affected lobe is a safer proceeding in the larger tumours whether malignancy is suspected or not. I am sure that before routine examinations were made many early cases of carcinoma were overlooked and that surgeons are not generally aware of the relative frequency of this condition. An example of this came to hand recently in a man from whom I removed what appeared to be a simple adenoma six years ago (Case 10). Fortunately I performed a lobectomy but did not have it examined. Early this year I removed a mass from well out in the side of his neck and the pathologist reported adeno-carcinoma of thyroid origin. If a tumour is extensive but relatively mobile, it should be removed with any involved musculature and even the recurrent laryngeal nerve if involved. At times it is difficult to free a mass from the trachea, larynx or oesophagus, but it should be pared off as closely as possible and deep X-ray therapy commenced within a week or ten days. If lymph gland metastasis has occurred it may be advisable to perform a block dissection but I do not carry this out as a routine in cases where the growth is apparently localized.

In the Lahey Clinic a much more optimistic view has been adopted with the extensive neoplasms (Cattell, 1946) and as much as possible of the growth is removed, tracheotomy performed and intensive irradiation instituted as soon as practicable. It is to be noted that they do not carry out a radical neck dissection in these extensive cases. While, on the whole, results in these late cases continue to be poor, there is an occasional long survival.

SUMMARY.

1. Carcinoma of the thyroid is much more common than is generally thought.

2. Age is no criterion as to its possible development.

3. It is most commonly found in association with or super-imposed upon a single adenoma in the thyroid. The incidence in males is nearly double that in females in these cases.

4. It is seldom met in association with acute thyrotoxicosis but some cases of carcinoma of the thyroid may present a low-grade chronic thyrotoxicosis.

5. It does occur occasionally in multinodular goitres and is usually evidenced by a rapid increase in growth with hardness in one area.

6. There are no reliable positive signs or symptoms to aid early diagnosis.

7. The best prophylaxis is early removal of all single adenomata irrespective of age and of the multiple adenomatous gland in which recent change has developed.

8. Excision of the affected area, lobectomy or even total thyroidectomy are the correct surgical procedures. Enucleation is to be avoided. Complete examination of the whole gland is advisable at operation.

9. In late stage cases without metastases resection of the tumour should be attempted and followed by deep X-ray therapy.

10. It b

11. In v w

12. A t X e o w

13. T o si se

14. It p th in p u sh

I Geoff sectio The Mr. V Medic and h of Cl Alfre are excell

BIELSC vol
BRANS vol
BRODE Su
CATTE pa
CHILD
COLE, vol

10. It is seldom necessary to carry out a block dissection of the cervical glands.

11. In the papilliferous carcinomata all involved glands should be removed along with a lobectomy on the involved side.

12. All cases except the papilliferous tumours should be given adequate deep X-ray therapy. Even in late stage cases, expectancy of life is increased and occasionally prolonged remission is met with.

13. The injudicious use of iodine in cases of adenomatous goitre may very possibly play a part in stimulating the onset of carcinoma.

14. It is most unlikely that "thio" compounds used for the control or cure of thyrotoxicosis will lead to the increase in carcinoma of the thyroid but all persistently enlarged glands after its use and all cases of toxic nodular goitre should be advised to undergo operation.

ACKNOWLEDGEMENTS.

I am indebted to Drs. A. H. Tebbutt, Geoff. Davies and V. J. McGovern for the sections and diagnosis of the various cases. The photomicrographs have been made by Mr. Woodward Smith of the Department of Medical Artistry, the University of Sydney, and by Mr. Len Johnson of the Department of Clinical Photography at the Royal Prince Alfred Hospital, Sydney, and my thanks are extended for their interest and the excellence of the work.

REFERENCES.

BIELSCHOWSKY, F. (1944), *Brit. J. Exp. Path.*, vol. 25, page 90.

BRANSON, K. M. and HOUSTON, W. (1949), *Lancet*, vol. 2, Page 979.

BRODERS, A. C. and PARKHILL, E. M. (1944), *Surgery*, vol. 16, page 633.

CATTELL, R. B. (1946), *West. J. Surg.*, vol. 54, page 444.

CHILDS, P. (1950), *Brit. J. Surg.*, vol. 37, page 274.

COLE, W. H. *et al.* (1945), *J. Amer. Med. Assoc.*, vol. 127, page 883.

CRILE, Geo., Jnr. (1949), "Practical aspects of thyroid disease." Philadelphia. W. B. Saunders.

DINSMORE, R. S. (1948), *Cleveland Clin. Quart.*, vol. 15, page 104.

DUNHILL, T. P. (1931), *Brit. J. Surg.*, vol. 19, page 83.

Editorial (1945), *J. Amer. Med. Assoc.*, vol. 127, page 278.

FOSS, H. L. (1938), *Surg. Gynec. Obstet.*, vol. 66, page 556.

FRIEDMAN, N. B. (1949), *J. Clin. Endocrinol.*, vol. 9, page 874.

GIBSON, E. W. and POATE, H. R. G. (1949), *Med. J. Aust.*, vol 2, page 151.

GOLDMAN, L. (1948), *Trans. Amer. Ass. Goiter*, page 224.

GRAHAM, A. (1924), *Surg. Gynec. Obstet.*, vol. 39, page 781.

—— (1925), *Ann. Surg.*, vol. 82, page 30.

HINTON, J. M. and LORD, J. W., Jnr. (1945), *J. Amer. Med. Assoc.*, vol. 129, page 605.

HODDLE, N. G. (1949), *Med. J. Aust.*, vol. 2, page 570.

KENNEDY, R. L. J. (1935), *J. Pediat.*, vol. 7, page 631.

LAHEY, F. H., HARE, H. F. and WARREN, S. (1940), *Ann. Surg.*, vol. 112, page 977.

LANGE, H. L. and MACLEAN, K. F. (1949), *Surgery*, vol. 26, page 862.

LOCKWOOD, A. (1947), *Trans. Amer. Ass. Goiter*, page 63.

MEISSNER, W. A. and LAHEY, F. H. (1948), *Trans. Amer. Ass. Goiter*, page 137.

PACK, G. T. and LIVINGSTONE, E. M. (1940), "Treatment of cancer and allied diseases." New York. Paul B. Hoeber.

PEMBERTON, J. de J. (1939), *Surg. Gynec. Obstet.*, vol. 69, page 417.

—— and BLACK, B. M. (1944), *Surgery*, vol. 16, page 756.

—— —— —— (1948), *Trans. Amer. Ass. Goiter*, page 163.

POATE, H. R. G. (1950), *Med. J. Aust.*, vol. 1, page 137.

RAMSAY, F. B. (1948), *J. Indiana Med. Ass.*, vol. 41, page 398.

RAWSON, R. W. *et al.* (1947), *Trans. Amer. Ass. Goiter*, page 187.

WARD, G. E., HENDRICK, J. W. and CHAMBERS, R. G. (1950), *Ann. Surg.*, vol. 131, page 473.

WARD, R. (1944), *Surgery*, vol. 16, page 783.

WARREN, S. (1940), *Amer. J. Roentgenol.*, vol. 46, page 447.

WARTHIN, A. S. (1929), *Proc. int. Assemb. postgrad. Ass. N. Amer.*, page 383.

WATSON, W. L. and POOL, J. L. (1940), *Surg. Gynec. Obstet.*, vol. 70, page 1037.

THE GENESIS OF VARICOSE VEINS.

By E. S. J. KING.

Melbourne.

He is deformed, crooked, old and sere,
Ill-fac'd, worse bodied, shapeless everywhere.
(The Comedy of Errors. Act IV, Sc. 2, l. 19.)

THE late results of varicosities of veins are frequently annoying to and sometimes serious for the patient, so that naturally attention is directed specially to these. Indeed, practically all discussions on varicose veins are limited to these results or at least begin with the stage when the phenomena of varicosity — lengthening, widening and tortuosity of the veins — have become well developed.

Probably because most often encountered, the phenomena observed in these "old and sere" structures are regarded as being the only significant ones and themselves the causes of the condition. The features of the early stages, and some which do not conform with current hypotheses of formation, are seldom mentioned. These, however, cannot be disregarded.

When these commonly overlooked features are considered closely, it is found that current hypotheses occupy a definite place amongst our ideas of the pathogenesis of varicose veins, but it is quite a different one from that usually accorded them. The problems are far wider than merely those of an aberration of venous channels; for example, the relationship of changes in veins to diseases of other parts of the circulatory system must be considered. Indeed, the scope for enquiry is even wider than this; just because the contents of tubes are different, it does not follow that their muscle coats are governed by different laws, so the relationship to conditions in other muscular tubes in the body should be considered.

Hypotheses of the origin of varicosities fall into two groups — the hydrostatic-morphological and the hydrodynamic. The former has been given great, often sole, consideration; the large amount of information which bears on the second has been consistently overlooked. The first group of hypotheses is considered now so that the field may be cleared for adequate discussion of the second.

THE FEATURES OF MATURE VARICOSITIES.

The phenomena that we associate usually with varicose veins are those that are to be seen best at the late stages. In many conditions it is the gerontic state which attracts attention and which is described by most writers. Nevertheless in these diseases attention has been directed with profit to the less characteristic forms or stages, and especially to origins.

In the present group, when the patient is seen first, grossly dilated veins which are usually irregular in diameter, with aneurysmal dilatations and irregularities of the walls, are present. The dilatation extends over considerable areas and may involve long lengths of vein up to and into the trunk. There is obvious incompetence of valves of the veins.

The site of varicosities is most frequently in the lower limb, in the haemorrhoidal region and in the pampiniform plexus. In these sites varicosities are often associated with symptoms or significant complications, which may explain their more frequent observation. Sometimes there is an obvious obstruction to a vein or series of veins, and in such cases emphasis is placed on this. Other features such as communications of superficial with deep veins in the limbs, high hydrostatic pressures and peculiarities (including reversal) of blood flow are not considered here in detail.

HYPOTHESES OF ORIGIN.

The hypotheses that have arisen round varicose veins afford a good example of the effects of the teleological approach which is so often adopted in medicine. The observations, irrespective of the stage of the

disease at which they are made, are transposed directly into aetiological factors. The easily made observations are (i) the veins are dilated; (ii) there is a high venous pressure and the blood in the affected veins (in a limb) is in direct continuity with that in the veins in the proximal part of the limb and the trunk; (iii) the valves are incompetent in the more dilated veins, and (iv) obstruction to the veins can sometimes be demonstrated and it may be very obvious.

As stated, we like to imagine that we know the final causes or the reasons for phenomena; thus these are quickly transformed (often without significant modification) into hypotheses of origin. Taking the various observations just mentioned in order, we can arrive at some direct "conclusions".

(i) Dilatation of the veins is the result of some change in the usual relationship between intravenous pressure and the state of the wall. The wall becomes thickened and, indeed, in thickness histologically resembles an artery. Such vessels are able to withstand high pressures. From the simple distension of the vessels it is clear that some change has occurred in the wall or that it is different from most vein walls. This is usually referred to as a "weakness" of the wall, and when the matter is pressed as to the nature of the weakness, this is said to be hereditary. Even if this were true, it would still be desirable to determine in what way the vessels of some individuals differ from others. Do these vessels lack muscle or elastic tissue, or is the muscle of a different kind? No evidence of anything of this kind is forthcoming. It is true that varicose veins are often found in several members of a family, but in view of the frequency with which it is found in the general population, such family incidence would be expected to occur. The writer has not been able to demonstrate any family incidence of statistical importance in an out-patient population, but in the literature considerable emphasis has been laid on familial examples (Curtius, 1928; Magnus, 1921; Ottley, 1934; Payne, 1936). No cognisance has been taken of other acquired factors which might be found in families; indeed, the hypothesis of a weakness of the vein walls of an hereditary type is pure speculation without any adequate support.

(ii) The high pressure in the affected veins may be assessed on theoretical grounds, but it can be measured readily and communication of the veins (in the thigh or leg) with those in the lower part of the abdomen is demonstrated daily in Trendelenburg's sign and the like. Furthermore, there is no doubt that many of the late features such as oedema and ulceration are related to this. It is a simple assumption that the increased pressure, responsible for the signs and symptoms which bring the patient for treatment, are the cause of the varicosity. Nevertheless it is sheer, and indeed unwarranted, assumption.

(iii) The incompetence of the valves can be demonstrated readily and, moreover, this is done daily in an out-patient department. The phenomenon is found in practically all, if not all, well developed varicosities. It is concluded, therefore, that the incompetence of the valves itself has given rise to the varicosities by allowing backflow of blood with the concomitant increased pressure. As will be discussed later, it can be demonstrated readily that the veins, in the early stages, have competent valves; these become ineffective only at the later stages.

(iv) Varicose veins are often divided into two main types — primary and secondary. The secondary form is that in which there is some definite obstruction to the veins above the varicosity, obviously playing a large part in its production. The primary type comprised those which develop without any evidence of obstruction.

The actual obstruction to a vein may be caused, for example, by a tumour or a thrombus. The close relationship in time between the development of these and the occurrence of the varices makes this a definite one. There can be no doubt in these cases that the rise in intravenous pressure is an important factor. Nevertheless that these cases constitute a special group different from the commonly observed ones is emphasized by their being designated "secondary". The secondary forms are important since their demonstrable relationship to venous obstruction is accepted, to some degree, as evidence that increased venous pressure plays a part in the development of varicosities of the primary type.

Here we see in action one of the frequently employed but thoroughly fallacious arguments of pathology and surgery. That what is true of one case or even one series of cases must necessarily be true of all others, is a misleading thesis.

From these and similar observations on the well developed stages of varicose veins certain hypotheses, which are usually accepted and quoted, have been developed. There is a weakness of the walls of the veins (probably hereditary) and varicosities develop because of loss of competency of valves which leads to a greatly increased intravenous pressure due to back flow from the proximal veins. It is apparent that these conclusions are a mixture of speculation and observations made on the late stages of the condition. This simple transference to the early stages is thoroughly unjustified without careful attention to the beginnings. These will be discussed here.

THE EARLY STAGES OF VARICOSE VEINS.

When the history of a patient with varices is taken carefully, it is found that usually at least some alteration in the veins has been present for a considerable time, that is, it is the usual thing to observe the later stages. The sudden onset of dilatation of previously unaffected veins is seen in pregnancy and in obstruction by tumours. These may give a history of dilatation at an earlier stage and many of the "primary" forms do give such a history.

When we come to consider the beginnings of the changes, therefore, it is important that we examine these cases at an early stage rather than attempt to deduce the nature of the early changes from consideration of the late stages. When this is done, several illuminating observations are to be made. These are, indeed, well known, but sufficient attention has not been paid to them.

(a) Varicose veins appear first almost always as a localized dilatation of some group — constituting a bunch of veins. These may occur in different places and without continuity with any obviously dilated veins. This collection of veins is sharply circumscribed, but communicates with veins which are normal in calibre. Thus between a bunch of veins near the knee and the groin, for example, there is a saphenous vein which is normal in calibre and in which the valves are demonstrably competent. Similar groups may occur in the thigh and the leg. These are mentioned specifically because it is to varicosities in the lower limb that the usually accepted hypotheses are supposed to apply.

(b) In the early stages the veins are slightly dilated, but not really varicose. The dilatation is associated with increase of muscle in the wall. This thickening of the muscle is an early development, and only after some time, after the early stages are past, is there atrophy and sacculation of the wall. These last, therefore, are not an integral part of the early process of dilatation.

(c) There is, however, even at an early stage, a swelling of the veins in the region of the valves. It is often assumed that such swelling is proximal to the valves — presumably a result of increased back pressure in the veins. This should then be due to the fact that the valves are competent — a contradiction of the idea that an important exciting factor is their incompetence. However, careful examination shows that the swelling of the vein is distal and not proximal to the valve. This cannot be explained easily on the notion of simple back pressure. The observation was made several years ago (Ledderhose, 1906, 1908).

(d) Pulsation is often present in these veins. In the early cases this cannot be due to back pulsation through the proximal veins because the valves are still competent, but in any case it can be tested by compression of veins such as the saphenous or femoral. This phenomenon was noted early in the century (Hasebrök, 1916; Ledderhose, 1908) and is discussed again.

(e) The blood in the veins can be shown to contain more oxygen than usual. Simple observation shows that the blood coming from an injured vein (for example, at operation) is often bright red in colour — indeed, resembling arterial blood. It is important that the observation of the blood of relatively newly developed varicosities be not confused with that of the venous blood of the long-standing examples. In these the blood is demonstrably venous in type with a small oxygen content. It is clear that there is a significant difference

in the blood content in the two circumstances, and this, apart from any other features, emphasizes that, in these two stages, we are here dealing with two quite distinct and different states of affairs.

FIG. I. Photomicrograph of a section of a varicose vein and adjacent tissue showing numerous vessels of capillary and larger size. (x 12)

(f) In the early stages the process is reversible. Occasionally a small bunch of veins will suddenly cease to be prominent. This does not occur often, but that it occurs at all is worth comment. This reversal may be associated with, say, termination of a pregnancy, and it should be mentioned here that this may occur at a stage when pressure cannot be the effective agent. Sometimes there is no obvious change in the physical state of the individual and certainly nothing in the adjacent or proximal vessels to suggest that some mechanical alteration is responsible.

(g) The histological appearances of the veins and the contiguous vessels are more prominent and certainly more significant than the usual, almost casual, description would suggest. The veins are certainly thickened with hypertrophied muscle coats, but the important feature is the vascularity of the adventitia.

In the outer coat and in adjacent tissues there are many large capillaries and small arterioles. These are either in small groups (Fig. I) or diffusely scattered in the adventitia (Fig. II). Sometimes the communication of these vessels with the vein may be demonstrable (Fig. III). These vessels are not found in this form in places other than at the site of the varicosity; for example,

they are absent from proximal undistended veins, nor are they seen usually in the region at a late stage of varicose formation.
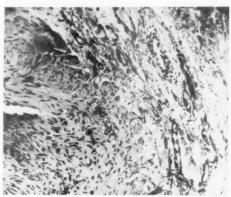

FIG. II. Photomicrograph of a section of the wall of a varicose vein showing vessels in the adventitia and adjacent tissue. (x 120)

Distribution of varicosities.

Varicose veins are to be found in almost every part of the body (Nicholson, 1923). Their frequent occurrence in the lower limbs distracts attention from the others. Varicosities of the haemorrhoidal veins and the pampiniform plexus are accepted because of their frequent occurrence, but also because their site allows them to conform with the general hydrostatic hypothesis. Varices at the gastro-oesophageal junction are said to be due to raised portal tension, but the more carefully these (Weinberg, 1949) and the "caput medusae" are considered, the less satisfactory is a mechanical explanation. In any case the changes in veins round large or rapidly growing tumours and the varices in the upper limbs and scalp demand some explanation other than a simple mechanical one.

None of the observations discussed above supports the idea of a simple mechanical mode of development depending on venous back pressure; indeed, though they show that there is an increased amount of blood in the vein, they suggest that this is of distal rather than proximal origin.

THE BASIS FOR HYPOTHESIS.

The alternative to the usually accepted morphological and hydrostatic hypothesis (that there is a weakness of the wall, that the valves are incompetent and that there is a high hydrostatic pressure) is the haemodynamic one. This is that there is a greatly increased flow into some part of the veins from the arterial side with increase in the amount of blood present for this reason. The hypothesis must go farther than this, since there is some dilatation of vessels. This is an old notion, but one that has not received adequate attention. It can be considered from two points of view.

FIG. III. Photomicrograph of a section of a varicose vein and neighbouring tissue showing numerous small vessels. The communication of one vessel with the lumen of the vein is shown. (x 6)

As early as 1669 Richard Lower stated that "it is an undisputed fact that the return of the venous blood is the result of the impulse given to the arterial blood and not of any attraction of the heart." A centripetal pulsation of the veins was observed by King in 1837. It was admitted (though with apparent reluctance) by Quincke (1868) and noted by Hippisley (1885). A centripetal pulsation was seen in veins in the frog's leg by Marshall (1831) and Palmer (1837). Dilatation of capillaries obviously facilitates this transmission of pulsation, and Lewis (1923) observed it after application of heat to the part. It was demonstrated also by White (1925). Using optical methods, Feil and Forward (1922) demonstrated a pulse in the portal vein of dogs.

That there were in some places communications between arteries and veins, of a diameter greater than the capillaries, was suggested at an early stage of knowledge of the circulation. As early as 1707 Lealis Leali stated that such were present in erectile tissues (Clara, 1927), and this was reiterated by Müller in 1835. Observations were made in animals by Paget (1850) and by Hyrtl (1862), and Sucquet (1862) described them in the skin of human beings. In 1877 Hoyer, by the use of various techniques, demonstrated the communicating vessels in several tissues of a number of animals. This work was elaborated by Grosser (1902) and Schumacher (1907), and more recently these arterio-venous anastomoses have been investigated by Grant (1930), Spanner (1931) and Clark and Clark (1934). These anastomoses occur in special areas as special organs, and are present usually as potential communications which become active, and thus apparent, in special circumstances. Thus in pathological conditions they are found to be more extensive in distribution than is appreciated in normal conditions.

That the rapid passage of blood from the arteries through arterio-venous communications might be responsible in many cases for the pulsation observed in veins was suggested by Quincke and Jürgensen (1920) and, indeed, is a matter of simple application of physical laws. It may, in some circumstances, be due to dilatation of capillary vessels so that their diameter (that is the combined diameters of a group) is such that the blood passes through easily. In other cases it is a matter of relaxation of the special anastomotic vessels mentioned. However, when vessels of capillary size become dilated for a period they develop the characters of larger vessels, so that the precise topographical features of the involved vessels need not detain us here.

Attempts have been made to study the phenomenon by production of artificial arterio-venous communications (Fischer and Schmeiden, 1909; Zancani, 1911), but changes observed thus do not help us to understand the beginnings of varicosities.

The development of increased blood flow with a visible pulsation in the efferent veins from a salvary gland when an increased flow of saliva is produced by stimulation of the chorda tympani was observed by Claude

Bernard (1358). A similar natural pheno-
menon is seen in the thyroid gland; gross
dilatation of the veins with centripetal pul-
sation is a feature of hyperactive states of
the gland. Dilatation of veins in and around
the periphery of tumours, particularly those
that are growing rapidly, is, as already
mentioned, a well known phenomenon.

FIG. IV. Photomicrograph of a section of peri-vascular
tissue showing a collection of vessels—capillaries and
arterioles. (x 90)

In all these circumstances it is clear that
there is some stimulus, affecting the local
condition of vessel walls or the blood flow,
responsible for the vascular change, and
there is no question of its being due (at
this stage) to some simple mechanical back
pressure. The development of new blood
vessels or increase in the local circulation
is due to a specific stimulus, often due
to tissue activity. Whatever the ultimate
factors, the immediate stimulus appears to
be of a chemical nature.

There is reason for a conclusion that in
some circumstances the chemical substances
may be of the nature of oestrogens. The
evidence is collected from various sources
and is of various kinds, but it affords a
considerable mass of information which
cannot be overlooked.

In the first place the relationship of
telangiectases of various forms to an excess
of oestrogens in the body is undubitable.
The association of these vascular peculiari-
ties with known conditions in which there
are endocrine disturbances, their develop-
ment in individuals with liver dysfunction,
when oestrogens are not metabolized — and
destroyed — as usual (Glass *et alii*, 1940),
and their development when individuals are

given oestrogens therapeutically (Bean,
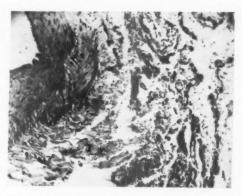1945), afford a clear indication of such
relationship.

FIG. V. Photomicrograph of portion of the wall of a
varicose vein showing vascularity of the adventitia.
(x 110)

Secondly, the effect of oestrogens on
smooth muscle in other organs is shown by
dilatation of the Fallopian tube following
their administration (Clauberg, 1938) and
the effect of such hormones on the ureter
(Hundley *et alii*, 1942). The dilatation of
the ureter in early pregnancy is not, as was
thought formerly, due to the pressure of the
enlarging uterus.
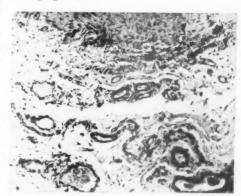

FIG. VI. Photomicrograph of the tissue adjacent to a
varicose vein showing numerous dilated vessels of
capillary size. (x 120)

Attempts to demonstrate a mechanical
obstruction has been unsuccessful, and as
long ago as 1920 Kidd suggested that the
dilated ureters in pregnancy was due to the
presence of some chemical substance in the

blood. Experimentally the administration of large doses of oestrone to mice was followed, as one of the earliest features, by distension of the urinary bladder and by hydronephrosis (Burrows and Kennaway, 1934; Lacassagne, 1933). Incidentally this occurred in both males and females. Some of the problems especially in regard to pyelitis of pregnancy have been reviewed by Burrows (1936).

That there is an active inhibition of the muscle of veins is shown by two observations. If a sufficiently strong stimulus be provided, the muscle is able to and will contract. This occurs when irritating fluids are injected therapeutically into the veins. On the other hand, although muscle is present in the wall, is histologically normal and, indeed, is increased in amount, its ability to respond to adrenalin is diminished (Läwen and Paulus, 1930). This inhibition of muscle activity is what is referred to as "the marked local effects of a progressive generalized inefficiency of the smooth muscle of the walls of the vein" by Delater and Hugel (1927).

Finally there are the observations regarding varicose veins in pregnancy. McCausland (1943) noted that in pregnant women with well developed varicose veins, (i) spontaneous abortion was less common than in others, (ii) that they showed abnormal endocrine features as indicated by body build, hair distribution and menstrual history, and (iii) varicose veins often developed during the pregnancy. He suggested that this might be due to the presence of excess progesterone. Agüro (1946) followed this suggestion by treating individuals complaining of symptoms from varicose veins with oestrogens, and found that there was considerable symptomatic improvement. It is clear that our knowledge of the precise actions of various hormones is still too uncertain to allow us to proceed far, but the general importance of the members of the oestrogen groups as influencing smooth muscle tone in some parts of the body is adequately demonstrated.

When all the phenomena are considered, we are presented with an hypothesis arising directly out of them. Varicose veins are to be considered in two stages which are separable and not necessarily related.

In the early stages there is a disturbance of the vascular relationships in an area resulting in an increased arterio-venous blood flow. This is associated with relaxation of the vessel walls not only of the arterio-venous communicating vessels, but in the veins themselves. This gives the greater blood flow in the veins, with the centripetal pulse, the oxygenated blood, the dilatation just distal to the valves, the reversibility (if the chemical conditions alter) and the histological appearances of the distended and numerous capillaries. It accounts for the localization of the condition with normal vessels to be seen proximal to the affected area.

When the condition has been present for some time, the changes become irreversible and progressive. To those already present are now added the hydrostatic factors. The valves become incompetent and, as with other disease processes, fibrotic and degenerative changes (not an integral part of the original process) appear. These are the ones which are so thoroughly and well described in most accounts. There is no need to review them here other than to point out again that these are late and secondary results and do not throw light on the original phenomena.

SUMMARY.

In review, at the early stage of varicosis there is in an area, a dilatation, sometimes of sudden onset, without valvular incompetence, with centripetal pulsation and without involvement of the proximal part of the veins. At this stage the veins are capable of contraction, that is, the muscle is not degenerate nor intrinsically weak; yet dilatation does occur.

These phenomena are explained by the action of some chemical factor, possibly a hormone or hormones of the oestrogen group, which have been shown to produce relaxation of smooth muscle in other tubes.

Once the condition has developed, then, just as with other structures such as bones, mechanical factors come into play and produce the various secondary changes which are clearly the effect of hydrostatic stresses. These give rise to the structures which are "ill-fac'd, worse bodied, shapeless everywhere."

The distinction between the two stages is of paramount importance in distinguishing between primary aetiological factors and those responsible for the more obvious and, in some respects, the more important secondary changes.

REFERENCES.

AGUERO, O. (1946), *Rev. obst. ginec., Caracas.,* vol. 6, page 155.

BEAN, W. B. (1945), *Medicine,* vol. 24, page 243.

BERNARD, Claude (1858), *C.R. Soc. Biol., Paris,* vol. 5, page 29.

BURROWS, H. (1936), *Proc. Roy. Soc. Med.,* vol. 29 (Comp. Med.), page 22.

BURROWS, H., and KENNAWAY, N. M. (1934), *Amer. J. Cancer,* vol. 20, page 48.

CLARA, M. (1927), *Ergebn. Anat. Entw. gesch.,* vol. 27, page 246.

CLARK, E. R., and CLARK, E. L. (1934), *Amer. J. Anat.,* vol. 54, page 229.

CLAUBERG, C. (1938), *Zbl. Gynäk.,* vol. 62, page 1034.

CURTIUS, F. (1928), *Dtsch. Arch. klin. Med.,* vol. 162, page 194.

DELATER, G., and HUGEL, R. (1927), *Rev. gen. Clin. Therap.,* vol. 41, page 166.

FEIL, H., and FORWARD, D. D. (1922), *Amer. J. Phys.,* vol. 60, page 312.

FISCHER, B., and SCHMIEDEN, V. (1909), *Frankf Z. Path.,* vol. 3, page 8.

GLASS, S. J., EDMONDSON, H. A., and SOLL, S. N. (1940), *Endocrinology,* vol. 27, page 749.

GRANT, R. T. (1930), *Heart,* vol. 15, page 281.

GROSSER, O. (1902), *Arch. mikr. Anat.,* vol. 60, page 191.

HALL, Marshall (1831), "A Critical and Experimental Essay on the Circulation of the Blood, Especially as Observed in the Minute and Capillary Vessels of the Batrachia and of Fishes." London: Sherwood, Gilbert & Piper.

HASEBRÖK, K. (1916), *Dtsch. Z. Chir.,* vol. 136, page 381.

—— (1916), *Pflüger's Arch. ges. Phys.,* vol. 163, page 191.

HIPPISLEY, J. (1885), *Nature,* vol. 32, page 389.

HOYER, H. (1877), *Arch. mikr. Anat.,* vol. 13, page 603.

HUNDLEY, Jr. J. M. DIEHL, W. K., and DIGGS, E. S. (1942), *Amer. J. Obst. Gynec.,* vol. 44, page 858.

HYRTL, J. (1862), *Nat. Hist. Rev., London,* vol. 2, page 99.

JURGENSEN, E. (1920), *Dtsch. Arch. klin. Med.,* vol. 132, page 204.

KIDD, F. (1920), "Common Infections of the Kidneys." London.

KING, T. W. (1837), *Guy's Hosp. Rep.,* vol. 2, page 104.

LACASSAGNE, A. (1933), *C.R. Soc. Biol., Paris,* vol. 113, page 590.

LAWEN, A., and PAULUS, G. (1930), *Dtsch. Z. Chir.,* vol. 225, page 5.

LEDDERHOSE, G. (1906), *Mitt. Grenzgeb. Med. Chir.,* vol. 15, page 355.

—— (1908), *Ibid.,* vol. 18, quoted by ROST, F. (1920), "Pathologische Physiologie des Chirurgiens (Experimentelle Chirurgie)." Leipzig: F. C. W. Vogel.

LEWIS, T. (1923), *J. Phys.,* vol. 58, page 21.

LOWER, R. (1669), *Tractatus de Corde item de Motu et Colore Sanguinis et Chyli in eum Transitu.* London: James Allestry, page 133.

MAGNUS, G. (1921), *Dtsch. Z. Chir.,* vol. 162, page 71.

McCAUSLAND, A. M. (1943), *West. J. Surg.,* vol. 51, page 199.

MULLER, J. (1835), *Muller's Arch. Anat. Phys. wiss. Med.,* page 202.

NICHOLSON, B. (1923), *Arch. Surg.,* vol. 7, page 47.

OTTLEY, C. (1934), *Brit. Med. J.,* vol. 1, page 528.

PAGET, J. (1850), "Lectures on Inflammation." London: Wilson & Ogilvy.

PALMER, J. F. (1837), The Works of John Hunter, F.R.S., with notes. London: Longman, Rees, Orme, Brown, Green & Longman.

PAYNE, R. T. (1936), *Brit. Med. J.,* vol. 1, page 877.

QUINCKE, H. (1868), *Berl. klin. Wschr.,* vol. 5, page 357.

v. SCHUMACHER, S. (1907), *Arch. mikr. Anat.,* vol. 71, page 58.

SPANNER, R. (1931), *Anat. Anz.,* vol. 71 (suppl.), page 24.

SUCQUET, J. P. (1852),"D'une Circulation dérivative dans les Membres et dans la tête chez l'homme." Paris: Adrien Delahaye.

WEINBERG, T. (1949), *Amer. J. Clin. Path.,* vol. 19, page 554.

WHITE, H. L. (1925), *Arch. Int. Med.,* vol. 35, page 124.

ZANCANI, A. (1911), *Arch. klin. Chir.,* vol. 96, page 91.

SOME PROBLEMS IN OESOPHAGEAL SURGERY.

By Douglas Robb.

Auckland.

MY observations are those of a general surgeon—as distinct from an endoscopist—and will concern the more general problems of oesophageal surgery rather than the details of operations for carcinoma. Though our clinical material is small by comparison with that of overseas units, we find each case worthy of detailed study. The further we travel the less do we experience that wonderful confidence with which we first attacked the gullet a few years ago by way of the chest. Anatomically, and in matters of anaesthesia and surgical technique we have made considerable progress, but results have too often been disappointing, and some of the difficulties seem insuperable.

Improvements in anaesthesia, especially the use of curare, have greatly facilitated both the abdominal approach to the hiatus, cardia and lower oesophagus, and also the thoracic approach. In general we have preferred the thoracic route to oesophagus, cardia, and many stomach lesions. Old and feeble patients tolerate it very well, and we rarely encounter pleural or pulmonary difficulties or sequelae. Antibiotics and post-operative care, doubtless help a lot here. The details of surgical technique are also important and we have had no troubles so far with the suture line in the form of early leakage or later stricture. We use interrupted non-absorbable sutures with knots on the lumen for the innermost layer, then interrupted mattress silk for the muscle, and finally supporting stitches between organs or from organ to pleural or other tissues to diminish tension and take weight. The gullet is never freed more than necessary, nor clamped nor cauterized near a proposed suture line. We have not used indwelling tubes regularly after operation but only on special indication. Oral feeding is given as soon as peristalsis is heard, usually twenty-four to forty-eight hours after operation. A good account of technique in oesophageal cases is given by McNeer (1949).

1. The Problem of Diagnosis.

Many factors conspire to make the exact diagnosis of oesophageal lesions difficult. Early symptoms in both simple and malignant lesions are slight and difficult to interpret, being easily attributed in error to spasms and other functional variations. The evaluation of what is seen with the endoscope and on fluoroscopy is likewise difficult, and I would stress that all possible sources of information be sought and considered together before diagnosis and treatment are determined. These include:—

(1) The clinical history. A first impression of a short history may stretch on inquiry back twenty years or more. Much can be learned by inquiring the effects of solids and liquids, hot food and cold, fatigue, posture, weather and emotional states. The patient can often localize on his sternum with considerable accuracy the site of an ulcer or obstruction, and the nature of his complaint may be almost diagnostic—for example, the sensation of filling and heaviness in cardiospasm, and the burning soreness of acid regurgitation into the lower gullet in acid oesophagitis and peptic ulcer of the gullet.

(2) The general state of the patients as regards colour, nutrition, skin texture, and loss of weight may be the most reliable single guide in differentiating a simple from a malignant condition (as in Case 3) or may be very misleading (Case 1). Progress under treatment such as that directed against anaemia, or periodic dilatation, comes under this heading.

(3) Fluoroscopy. On the whole I have found this, in good hands, a more helpful procedure than endoscopy in equally good hands. The contrast medium is watched in its descent and the gullet may be distended by an effervescent draught showing which

parts of its wall are elastic and which rigid. Mucosal patterns are studied for distortion and ulcer niches. The relation of the junction of the oesophagus and stomach to the diaphragm is noted in the erect posture, and also in the head-down position with or without pressure on the upper abdomen, in order to gauge the state of the hiatus in the diaphragm. Repeated fluoroscopy is better than relying on films taken elsewhere. Extreme thoroughness and vigilance in this work is essential. I have known a good radiologist miss a hiatus hernia not only before it had been demonstrated elsewhere, but also afterwards when the patient returned and sought confirmation.

Brick (1949) gives hiatus hernia as the second commonest lesion (after duodenal ulcer) in the radiological diagnosis of the upper gastro-intestinal tract. It frequently has other lesions associated with it and much care is required in appraising the cause of symptoms.

(4) Endoscopy. Not practising t h i s method myself I freely confess to a difficulty in interpretation of things seen. No one could miss the haemorrhagic type of acid oesophagitis at the lower end, but the evaluation of ulcers seen, with or without biopsy, and the difficulty, at times, of correlating them with fluoroscopic findings, is considerable. Although, short of serious troubles such as perforation which have been known to follow oesophagoscopy, the procedure at times upsets the patient considerably, I feel that this method should be used and repeated in almost every case.

(5) Direct examination after thoracotomy. This method may justifiably be used when all preceding evidence put together is inconclusive, or leaves dangerous doubt at large. It may be merely a last confirmatory step in a confident diagnosis. It can include external inspection and palpation of

stomach and cardia through a split in the diaphragm, and the gullet at least up to the root of the lung or the arch of the aorta. The perioesophageal infiltration and adhesion of a peptic ulcer, together with the hard, rigid gullet wall extending some distance beyond the actual ulcer, must be seen and felt to be believed. The carcinomatous mass and metastases in glands are usually unmistakeable. A final stage in this examination is the deliberate inspection of the mucosa of the gullet either at and about a proposed point of section for removal, or by special incision. In simple strictures and tumours, and especially in malignant tumours, neither the fluoroscopic guide to a safe level of section, nor the outward feel, are enough. Even after direct inspection, one sometimes wants the help of frozen section biopsy. The latter might have saved a patient (Case 24) from local recurrence and death, whereas in another patient (Case 4) the line of section had to be made a second time higher up, because of the misleading impression gained by external palpation.

2. THE PROBLEM OF CARDIOSPASM.

Only those cases are included where the long history, the grossness of the obstruction, the size of the oesophagus and the damage to its lining, the choking or the loss of weight, has led to the performance of a major operation for the relief of the obstruction.

The first 5 of our 7 cases have been described previously (Aickin, J. Hardie Neil and Douglas Robb, 1934; Douglas Robb and E. I. A. Macdonald, 1946; Douglas Robb and Rowan Nicks, 1948). The first 2 (Cases 16 and 17) had oesophago-gastrostomy by the abdominal route, and remain well after eighteen years and five years respectively. There has been adequate relief of obstruction and discomfort, nutrition has improved, and all symptoms ameliorated. The gross size of the gullet has not diminished much. There have been no symptoms of herniation, nor of reflux, nor of acid oesophagitis or ulcer at the lower end.

The subsequent series of 5 cases (Cases 18-22) all had cardioplasty by longitudinal incision into gullet and stomach with transverse suturing done through the chest at times varying from two and a half years to nine months ago. The hiatus was enlarged to allow of the operation and its edges loosely stitched to the stomach wall, so that a degree of herniation was an inevitable result. Healing and post-operative convalescence was good in all cases, and all have been relieved of obstructive symptoms. Results of these cases are recorded later.

Case 18.

I.S. female. Gross cardiospasm; symptoms for sixteen years: Trans-thoracic cardioplasty two and a half years ago. Patient reports herself recently as in "very good condition with no symptoms whatever."

Thirty-one months later had no clinical complaints at all. Radiologically there was still a greatly dilated oesophagus with a sigmoid loop to the R. which seemed to guard against reflux in the Trendelenburg position. There was little or no delay in material passing downwards and no suggestion of peptic ulcer. Not much of the stomach lay above the diaphragm.

Case 19.

F.W. male aged 75. Very gross cardiospasm for many years. Poor general condition, wasting and auricular fibrillation. Two and a half years ago trans-thoracic cardioplasty after much preparation. Tolerated well. Relief of obstruction: general condition remains poor.

Case 20.

E.R. female aged 40. Gross cardiospasm over ten years. Trans-thoracic cardioplasty two and a half years ago. Four months later, onset of regurgitation and oesophagitis; ulcer seen in X-ray. Blood transfusion required for anaemia. Six months ago second operation to replace all stomach below diaphragm. This appeared to relieve her almost completely until very recently when a moderate haematemesis occurred. Radiologically the cardia was below the diaphragm, and no hernia nor ulcer niche was demonstrable. The gullet was smaller, but reflux of contents was free.

Case 21.

R.C.O. female aged 39. Dysphagia for years — gross cardiospasm. Two years ago trans-thoracic cardioplasty. Obstruction completely relieved but from soon after operation persistent symptoms of acid oesophagitis; later, haematemesis. Shallow ulcers plus oesophagitis seen on endoscopy. Remains fairly comfortable on suitable diet. Result poor.

Case 22.

A.M.C. female aged 61. Dysphagia for four years; gross dilatation and oesophagitis. Six months ago trans-thoracic cardioplasty. Relief from obstruction but symptoms of regurgitation and oesophagitis. No evidence of anaemia or ulcer. Nine months later complete relief of obstruction but some burning substernal pain. On fluroscopy reflux was seen, and signs of oesophagitis, but no ulcer niche.

In these 7 cases, there are no excellent results, there are 4 fair to good results, 1 doubtful, and 2 in which general health is seriously threatened by acid regurgitation, ulceration, and haemorrhage — the same syndrome that we will meet under hiatus hernia.

Other writers have expressed dissatisfaction with some or all of the recognised procedures.

Maingot (1949) allows cardioplasty, oesophago-gastrostomy and Heller's operation of extra-mucous oesophago-cardiomyotomy, but strongly favours the latter, as being simple to do, and devoid of immediate or late sequelae such as regurgitation, oesophagitis or peptic ulceration.

Edwards (1950) allows Heller's operation only, using at least a two inch incision, the operation being done from the abdomen. He has had "uniformly successful" results in 15 cases.

Barrett - Franklin (1949) likewise favour Heller's operation by either the thoracic or abdominal route, and have had good results in 10 out of 11 cases. This was after an unhappy experience in 19 cases of oesophago-gastrostomy (and also with other cases of cardioplasty) where the great majority suffered more or less severely with regurgitation and acid oesophagitis and ulcer.

Allison (1946) had "complete success" with Heller's operation in all of 19 cases, and d'Abreu (1950) "good results" in 11 out of 12 cases.

Brock (1950) had both good and bad results with both oesophago-gastrostomy and Heller's operation.

Failures after Heller's operation are referred to by Redon and Lacoste (1949) and by d'Allaines et al. (1949), the latter group advocating simultaneous vagotomy with

Heller's operation, and partial gastrectomy with phrenic crush for a failed Heller's operation.

Delannoy (1949) had good late results in Heller's operation in 12 out of 14 cases, but admitted unpredictability.

Wulff and Malm (1949) had poor results with Heller's operation, but better with cardioplasty leaving a portion of stomach above the diaphragm. Anaemia was the chief trouble with the latter cases.

Sweet (1947) favoured cardioplasty without effort to replace stomach below the diaphragm nor attempt to make a tight closure of the hiatus. He had good results, the only frequent complaint being heartburn and regurgitation. I have not been able to find any later expression of view by this writer.

Ochsner and de Bakey (1941) and Clagett et al. (1945) write strongly in favour of oesophago-gastrostomy carried out by the abdominal route, and this seems to be the present procedure in United States of America. No reference is made to the possibility of regurgitation and acid oesophagitis, nor to the desirability or otherwise of ensuring the competence of the cardia. I have not found references to late results of these cases.

It is not to be wondered at therefore, that Moersch (1948) makes a plea for caution in using major surgical measures until the use of dilators has proved a failure, and warns that, with all known methods of operation, some proportion of symptoms are likely to remain.

Personally I have two doubts about Heller's operation—

(1) In performing cardioplasty we have seen on two or three occasions a mucosal web at the narrowest portion, not unlike a poorly marked perforated diaphragm as seen in a coarctation of the aorta. Perhaps this sometimes prevents the mucosa bulging sufficiently after the muscular wall has been divided, and so obstruction remains.

(2) Granted adequate relief of obstruction, there seems little to prevent reflux, oesophagitis and ulcer as after cardioplasty, unless the hiatus is and remains competent, or is made so, against reflux. For this reason the abdominal approach might be better if one could be sure of the hiatus; if not, the thoracic, because we feel we can gauge its size better from above, and also tighten it to the required degree.

Simultaneous vagotomy, with Heller's operation, seems fraught with risks of spastic and ulcerative sequels in the oesophagus and of dilatation postoperatively in the stomach (Wulff and Malm, 1949; Barrett and Franklin, 1949).

I therefore propose to deal with advanced cardiospasm in the future by Heller's operation with attention to adequate mucous bulging, and to the competence of the hiatus. Serious ulceration and bleeding will call for resection of the affected part of the gullet and oesophago-jejunostomy, with or without partial gastrectomy. But I will be even more conservative in my acceptance of patients for major operation than in the past, for it does little service to the patient to replace obstruction by incompetence and regurgitation which carry different but possibly more serious risks.

3. THE PROBLEM OF THE INCOMPETENT CARDIA.

We have already encountered this under cardiospasm after operative relief of the obstruction; it occurs under many other circumstances both before and after operations of many kinds on the oesophagus and cardia. Any condition in which the normal barriers to reflux of acid gastric juice up into the lower oesophagus are broken down, may lead to distressing symptoms, serious ill-health, and even loss of life.

The normal barriers are some intrinsic neuro-muscular control in the wall of the lower end of the oesophagus, the acute angle between the distended fundus and the oblique entrance of the gullet, and the "pinch-cock" of the muscular gap in the right crus of the diaphragm. The unpleasant burning sensation caused by even momentary contact of acid gastric contents with the lining of the lower oesophagus during regurgitation and

vomiting is familiar to everyone. The endoscopic appearance of acid oesophagitis is also very familiar with its red angry thickened mucosa which bleeds on the lightest touch. The later stage of actual ulceration, shallow and acute, or deep penetrating and chronic, with peri-oesophagitis or perforation, is also well known. Oesophagitis with or without ulceration frequently leads to profound anaemia, either from repeated unrecognised haemorrhages or from one or more attacks of severe haematemesis or melena. It is so troublesome a complication of oesophageal or diaphragmatic lesions or operations that it outranks jejunal ulcer in gastro-enterostomy in former times.

In some situations, loss of all three barriers is inevitable. Resection of the cardia, with or without sizeable portions of gullet or stomach as well, and oesophago-gastrostomy at a level to which the diaphragm cannot reach, creates such a situation, whether the original lesion be simple stricture or ulcer of oesophagus, or growth.

Incompetence, reflux, and oesophagitis must be reckoned with, and the surprise comes when they do not cause trouble. Cases 4, 23 and 24 are examples of this, though perhaps in no instance has the follow-up been long enough. The child whose history is set out in Case 4 has no symptoms nor signs on fluoroscopy and can be held up by her heels and shaken without regurgitation. It may be that the effect of the vagotomy, implicit in the resection, diminishes the acid secretion sufficiently in many cases but Brock (1942) and Allison (1946) refer to the occurrence of peptic ulcer after resection for cancer, and Borrie in a personal communication says he has seen eight strictures (presumably following ulceration) after oesophago-gastrostomy for cancer.

Experiments on post-mortem and animal material suggest that there may be some virtue, in these cases, in making a flap of gastric mucosa under the oesophageal opening to act as a check-valve against regurgitation. Certainly it appears to be mechanically effective and the best of numerous methods tried. I have not had the opportunity to apply it to a patient. It might be done as the last stage in an oesophago-gastrostomy, through a slit in the fundus of the stomach; or perhaps better as a separate

and later procedure in the treatment of serious regurgitation. The alternative would be to alter the anastomosis to an oesophago-jejunostomy, with or without removal of the stomach. More recent opinion seems to favour retention of the excluded stomach and the use of the Y-loop (Roux) of jejunum.

In the case of hiatus hernia with peptic ulcer of the oesophagus, the situation may be different in that it may be possible to restore the stomach to the abdomen and recapture an effective barrier in the form of a tightened and reinforced pinch-cock. In Case 7, in spite of unpromising anatomical and pathological features, this was done with at least early success. Cases 5 and 6 were bad cases treated by cardioplasty in the initial stages of our experience with a good result in 5 and a bad one in 6. One suggestion to aid in strengthening the narrowed hiatus is to use a fibro-muscular graft from the diaphragm stitched round the gullet. This seems promising from post-mortem studies but has not been needed in our latest hiatus repairs. Often the muscular tissue in the crus to the left and posterior aspects of the gullet is unpromising after suture, and this graft would reinforce it.

In the really bad cases of peptic ulcer with serious bleeding and obstruction, and shortening and stiffening of the gullet wall, it may be quite impossible to restore the normal anatomy, and resection of the junction must be carried out. Oesophago-jejunostomy without resection of the stomach is advocated confidently for this by Allison (1949). This should be done in Case 6, but has not yet been carried out. At least 2 of our cardiospasm cases (Cases 20 and 21) are also candidates for this procedure.

SUMMARY.

The problems of exact diagnosis, the correct treatment of advanced cardiospasm, and the management of acid regurgitation leading to oesophagitis and peptic ulcer are discussed.

It is suggested that it is necessary to use all available methods of diagnosis before deciding on treatment. That while Heller's operation with certain safeguards is probably the best procedure for advanced cardiospasm, it is not wholly reliable, and should

not be resorted to lightly. That a flap of gastric mucosa might be useful in checking r e f l u x after resection and oesophago-gastrostomy. That a graft of diaphragmatic tissue might be useful in the fortification of an otherwise doubtful repair of a hiatus hernia.

ACKNOWLEDGEMENT.

TABLE I.

PROBLEMS IN OESOPHAGEAL SURGERY.

MATERIAL FOR STUDY.
26 CASES.

	Totals
SIMPLE STRICTURE Cases 1, 2, 3	3
CHEMICAL STRICTURE Case 4	1
HIATUS HERNIA	
With Oesophageal Ulcer Cases 5, 6, 7	
Without " " Cases 8, 9,	11
10, 11, 12, 13, 14 and 15	
CARDIOSPASM	
Oesophago-Gastrostomy (Abd.) Cases 16, 17	2
Trans-Thoracic Cardioplasty Cases 18, 19, 20, 21 and 22	5
CARCINOMA	
Cardia and Stomach Cases 23 and 26	2
Middle and lower third of oesophagus Cases 24 and 25	2
TOTAL:	25

APPENDIX ON CLINICAL MATERIAL.
BRIEF SUMMARY OF CASE RECORDS.

1. SIMPLE STRICTURE.

Case 1.

H. H. McK. Female aged 72. Severe annular stricture 1½ inches above hiatus, with 28 pounds loss of weight. Twelve months' history.

While being prepared for operation died suddenly for no clear reason.

At autopsy a simple stricture with minimal ulcer. Cause undetermined—a very slight lesion indeed from the pathologist's point of view.

Case 2.

G. O. Male aged 10. Extensive oesophagitis with intractable stricture formation of unknown aetiology. Resection and oesophago-gastrostomy beneath aortic arch. Post-operative death from shock.

Case 3.

C. E. B. Male aged 72. Ulceration and stricture in last 2 inches of the oesophagus with small gastric herniation. Duration of symptoms was three years. Treated satisfactorily by dilatation. Cause of original ulcer and scarring uncertain— ? ectopic gastric mucosa, ? congenital short oesophagus.

2. CHEMICAL STRICTURE.

Case 4.

A. T. Female aged 4. Caustic soda burn—extensive stricture—false passage—mediastinal abscess —communication with bronchus and later bronchiectasis of left lower lobe. Resection—dislocation of oesophagus to left of aortic arch — oesophago-gastrostomy—left lower lobectomy; now symptom free—no regurgitation nor suggestion of ulcer.

3. HIATUS HERNIA WITH PEPTIC ULCER OF OESOPHAGUS.

Case 5.

W. H. Male aged 76. Severe peptic ulcer with dysphagia and obstruction—short history simulating that of carcinoma. Cardioplasty; good result two years later in spite of residual hernia.

Case 6.

R. W. Female aged 64. Severe peptic ulcers for 2-3 inches above lower end with short history and obstruction. Cardioplasty. Two years later fairly well no obstruction; but major trouble requiring blood transfusion from haemorrhage and anaemia, quiescent for last three months.

Case 7.

M. W. Female aged 67. Irreducible hernia with gross ulceration of lower end of oesophagus and obstruction. Mobilization and closure of hiatus with difficulty around oesophagus, and reduction of stomach to abdomen. Immediate result good in all respects including fluoroscopic appearances.

4. HIATUS HERNIA.

Case 8.

F. W. S. Male aged 38. Moderate sized hernia with rather severe symptoms for three years — repair—cure (operation done eighteen months ago).

Case 9.

A. S. Female aged 54. Moderate sized hernia of sliding type originating twenty years before in second pregnancy. Dyspeptic symptoms unrelieved by cholecystectomy (no stones found). Repair. Good early result.

Case 10.

E. P. Female aged 67. Moderate sized hernia—symptoms of dysphagia two months. Repair. Good result three months later.

Case 11.

G. D. Female aged 61. Small hernia. Repair. Symptoms relieved.

Case 12.

M. C. Female aged 56 years. Two years history of severe symptoms including major haematemesis. Repair. No symptoms of ulcer. Good result six months later.

Case 13.

I. B. Female aged 60. Severe symptoms of vomiting and haematemesis; short history. Para-oesophageal hernia repaired. Complete cure twelve months later.

Case 14.

E. G. Female aged 59. Short history of dysphagia for seven months. Repair sixteen months ago; hernia of paraoesophageal type. Symptoms now absent but partial recurrence of hernia seen on fluoroscopy.

Case 15.

M. C. Male aged 49. Severe symptoms of five months duration. Moderate hernia of sliding type. Repair. Radiological cure but dyspeptic symptoms persist; cause not ascertained.

5. CARDIOSPASM.

Case 16.

D. F. Male aged 71. Very gross cardiospasm for many years. In 1931, when aged 52, abdominal oesophago-gastrostomy performed, now, 19 years later, reports himself hale and hearty with only minor discomfort provided he masticates carefully, but seven years ago required some gullet lavage.

Case 17.

K. W. S. Male. Gross cardiospasm for many years with increasing trouble.

Four and one half years ago abdominal oesophago-gastrostomy; good or very good result to date — occasional symptoms if dietary indiscretions are committed and on change of weather but weight and activity maintained.

Case 18.

I. S. Female. Gross cardiospasm, symptoms for sixteen years. Transthoracic cardioplasty two and one half years ago. Patient reports herself recently as in "very good condition with no symptoms whatever."

Case 19.

F. W. Male aged 75. Very gross cardiospasm for many years. Poor general condition, wasting and auricular fibrillation. Two and one half years

ago transthoracic cardioplasty after much preparation. Tolerated well. Relief of obstruction: general condition remains poor.

Case 20.

E. R. Female aged 40. Gross cardiospasm over ten years. Trans-thoracic cardioplasty two and one half years ago. Four months later, onset of regurgitation and oesophagitis; ulcer seen in X-ray. Blood transfusion required for anaemia. Six months ago second operation to replace all stomach below diaphragm. This appeared to relieve her almost completely until very recently when a moderate haematemesis occurred.

Case 21.

R. C. O. Female aged 39. Dysphagia for years —gross cardiospasm. Two years ago trans-thoracic cardioplasty. Obstruction completely relieved but from soon after operation, persistent symptoms of acid oesophagitis; later, haematemesis. Shallow ulcers plus oesophagitis seen on endoscopy. Remains fairly comfortable on suitable diet. Result poor.

Case 22.

A. M. C. Female aged 61. Dysphagia for four years; gross dilatation and oesophagitis. Six months ago trans-thoracic cardioplasty.

Relief from obstruction but symptoms of regurgitation and oesophagitis. No evidence of anaemia or ulcer.

6. CARCINOMA.

Case 23.

J. H. W. D. Male. Carcinoma at the cardiac end of the stomach. Trans-thoracic resection and oesophago-gastrostomy. Good progress, six months later. No dysphagia, no obstruction, no suggestion of ulceration or stricture.

Case 24.

C. de St. C. G. Male. Carcinoma lower third of oesophagus. Resection and oesophago-gastrostomy after dislocation of oesophagus to left of aorta. Good progress for five months when dysphagia and radiological sign of recurrence in suture line, gullet having been divided too near the growth. Resection of recurrence tolerated well but early decline and death from secondaries.

Case 25.

McK. Female. Carcinoma lower third of oesophagus. Resection and oesophago-gastrostomy after dislocation of oesophagus to left of aorta. Early trouble with gastric dilatation. Died on fourth day of cardiac arrhythmia and failure. A promising case—only one gland seen, closely adherent to oesophageal wall.

Case 26.

J. R. Male. Carcinoma of cardia. Resection and oesophago-gastrostomy. Recent case. Good immediate result.

REFERENCES.

AICKIN, C., NEIL, J. Hardie, and ROBB, D. (1934), *Aust. N.Z.J. Surg.*, vol. 3, page 384.

ALLISON, P. R. (1946), *Proc. Roy. Soc. Med.*, vol. 39, page 415.

—— (1949), *Lancet*, vol. 2, page 91.

BARRETT, N. R., ALLISON, P. R., d'ABREU, F. A., and BROCK, R. C. (1950), *Brit. Med. J.*, vol. 1, page 179.

—— and FRANKLIN, R. H. (1949), *Brit. J. Surg.*, vol. 37, page 194.

BRICK, I. B. (1949), *Arch. Surg.*, vol. 58, page 419.

BROCK, R. C. (1942), *Brit. J. Surg.*, vol. 30, page 146.

Case Records (1950), *New Engl. J. Med.*, vol. 242, page 186.

CLAGETT, O. T., MOERSCH, H. J. and FISCHER, A. (1945), *Surg. Gynec. Obstet.*, vol. 81, page 440.

D'ALLAINES *et al.* (1949), *Mém. Acad. Chir.*, vol. 75, page 511.

DELANNOY, E. (1949), *Mém. Acad. Chir.*, vol. 75, page 629.

EDWARDS, R. (1950), *Lancet*, vol. 1, page 24.

MCNEER, G. (1949), *Surgery*, vol. 26, page 590.

MAINGOT, R. (1949), *Post-grad. Med. J.*, vol. 26, page 197.

MOERSCH, H. J. (1948), *Gastroenterol*, vol. 12, page 520.

OCHSNER, A. and DE BAKEY, M. (1940), *Arch. Surg.*, vol. 41, page 1146.

—— —— (1941), *Surg. Gynec. Obstet.*, vol. 72, page 290.

REDON, H. and LACOSTE, J. (1949), *Mém. Acad. Chir.*, vol. 74, page 504.

ROBB, D. and MACDONALD, E. I. A. (1946), *Aust. N.Z.J. Surg.*, vol. 15, page 221.

—— and NICKS, R. (1948), *Aust. N.Z.J. Surg.*, vol. 18, page 133.

SWEET, R. H. (1947), *Surg. Clin. N. Amer.*, page 1128.

WULFF, H. B. and MALM, A. (1949), *Thorax*, vol. 4, page 243.

THE MODERN APPROACH TO DEVELOPMENTAL ABNORMALITIES.

By IDA MANN.

Perth.

T HE fertilized human ovum weighs .005 mg. Forty-four ce!l divisions occur before birth producing fifteen million million cells weighing 3000 g. After birth only four more cell divisions are required to convert the new born to the adult body. When we think of this complicated process with its thousands of mutual interactions and adjustments, which at any stage may show aberration, we can but feel surprised by the advent of a normal individual and by the relative infrequency of congenital anomalies.

As clinicians we are concerned with developmental abnormalities in four ways; first, we must be able to diagnose them (this is usually easy but may present problems in the case of post-natal developmental aberrations); second, we must be able to advise as to treatment, if any be possible; third, we must make some attempt to assess the possible cause and, fourth, we must be able to give at least tentative advice about the possibility of abnormality in future members of the family.

The question of diagnosis is not suitable for detailed discussion here since our skill in this field will depend on our knowledge of normal embryology, of reported and observed cases and also of the broad outlines of clinical classification of the main types of anomaly. Since all abnormalities depend on an aberration of normal growth at a definite stage they are bound to fall

into fairly well defined categories, though each case will show individual minor peculiarities.

With regard to treatment certain principles must always guide us. First, can surgery do anything to remedy the defect? This may be either by restoration or improvement of function or by cosmetic operation. Second, can we improve our patient's chances of adaptation to his disability by advice on education and on the correct psychological approach by the parents? The question of operation will always be an individual one. Certain defects, such as congenital coloboma of the eyelid or complete cleft palate demand early operation for essential restoration of function, in the first case to prevent drying of the cornea and ulceration, and in the second to facilitate feeding. Total congenital cataract also falls into this category since central fixation will not develop if operation is delayed too long. Certain other defects such as buphthalmia are surgical emergencies since they are progressive in themselves and, if untreated, will pass on to further loss of function. Other defects, however, may be unamenable to improvement but still should be operated on early, sometimes for cosmetic reasons, for example, arhinencephaly unilateralis, and sometimes to relieve the patient of discomfort, such as is inevitable for instance with a large congenital cystic eye over which the lids will not entirely close. Other unsightly but nonprogressive deformities such as unilateral microphthalmia or corneal dermo-lipoma may be left until the child is older, but should be dealt with if possible before school age, while other minor defects such as unilateral corneal nebulae or accessory

FIG. I.   Coloboma of eyelid.   A. Upper Lid.   B. Lower Lid.
(from Ida Mann "Developmental Abnormalities of the eye." C.U.P.)

auricles may be left until the patient him-self seeks advice. Each case must be con-sidered on its merits.

he has, "strain" may lead to further deteri-oration. This conception of "eye strain" is a somewhat nebulous one and leads some-times to such ano-malies of treat-ment as prohibi-tion of reading and close work to children with microphthal-mic eyes showing a myopic refrac-tion. In these cases the myopia is due to the sphericity of the lens and the high curve of the cor-nea and not to increased axial length likely to be accompanied by choroidal stretch-

FIG. II. Arhinencephaly unilateralis.
(from Ida Mann "Developmental Abnormalities of the eye" C.U.P.)

The education of the parents of a child suffering from a deformity which limits function forms an important part in treat-ment. The average layman finds it very difficult to realize what the defect means to the child and to understand that deprivation through congenital deformity will not have the same limiting or frustrating effect as would the same deprivation occuring in an adult previously normal. Thus the mental state of a completely anophthalmic child of normal mentality will be quite different from that of a patient who suddenly becomes blind, and quite different explanations and approaches are necessary, since in the former case so many words and phrases in everyday language are meaningless and the spatial perceptions and memories are of a different order, mental visualization being impossible. The greatest difficulty encountered is perhaps the over-protective parent and unfortunately the over-anxious doctor is not unknown as well. He too often plays an augmenting part in producing a kind of family anxiety neurosis. He may also, by curtailing the possible activity of the patient, prevent the full development of capabilities. Perhaps the best example of this type of family situation is to be found where the child is partially sighted. Often both doctor and parent fear that by encouraging the child to make as full use as possible of what sight

ing. Close work can often be accomplished by these children with ease, while distance vision even with full correction, is always poor. There can be no possible justification for curtailing use of the eye in these cases. Indeed they often have a greater amplitude of convergence than normal and there is no reason why the book should not be held in the optimum position close to the eyes. Also the modern approach to the question is in the direction of developing to the full the capabilities of each case. Even in cases where the fear of deterioration on use may have some basis (though these are much rarer than was previously thought) it is justifiable to allow full use of the eyes, since much will be learned during the formative years which will be of use later if deteriora-tion does occur. There is indeed no scientific evidence that use of a malformed but not diseased sense organ can hasten its deteriora-tion. We do not prohibit attempts to hear by partially deaf children: all modern treat-ment is towards educating what hearing remains, and the same trend is now becoming apparent in dealing with other sensory abnor-malities.

CAUSATION.

It is in the direction of assessment of cause that perhaps the greatest advances have been made. Animal experiment, study

of genetics and clinical observation have all played their part in giving us a clearer concept of the various ways in which a developing zygote may go wrong. Broadly speaking, abnormal development may be classified as:—

1. Genetic in origin, arising potentially at fertilization, but becoming apparent at some definite developmental stage, sometimes post-natal.

FIG. III.   Fibro-lipoma of cornea.

2. Genetically determined but environmentally produced, i.e., carrying a genetic constitution which will react to certain environmental factors in an abnormal way, but which, if they are absent, will result in a normal individual.

3. Purely environmental in origin, i.e., due to interference with the development of a normal zygote by abnormal outside influences.

4. Sporadic, by which is meant that the cause is unknown. In this group would

fall genetic characters arising as new mutations or through the fortuitous mating of two recessives showing

FIG. IV.   Dermo-lipoma of cornea.

FIG. V.   Filiform adhesion between upper and lower lids, very easy to remedy at any age.

It ment any old condi

FI sm

determ is no menta from phtha truly retini are a guecu macul senile cally termi

normal pedigrees, and also environmentally determined conditions so far not suspected.

It must be understood that a developmental condition may become manifest at any age, pre-natal or post-natal or even in old age, since certain senile degenerative conditions can be shown to be hereditarily
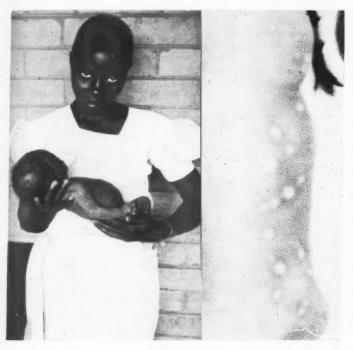

FIG. VI. Rhodesian native woman with new born child showing healed smallpox scars. The child was born on Nov. 1st, 1945. The mother had alastrim in Aug. 1945.

determined. The term "congenital anomaly" is not therefore synonymous with "developmental anomaly." Taking again examples from ophthalmology, coloboma iridis, microphthalmia and persistent hyaloid artery are truly congenital, while coronary cataract, retinitis pigmentosa and juvenile glaucoma are adolescent in time of onset, and pinguecula, arcus senilis, and some cases of macular degeneration and of cataract are senile in time of appearance although genetically and therefore developmentally determined.

All developmental anomalies can be studied from two aspects, that of their causal genesis (i.e., genetic versus environmental) and that of their formal genesis by which is meant the mechanics of production of the defect, the time at which development first became abnormal and the series of changes of gross shape and histology which resulted in the complete anomaly.
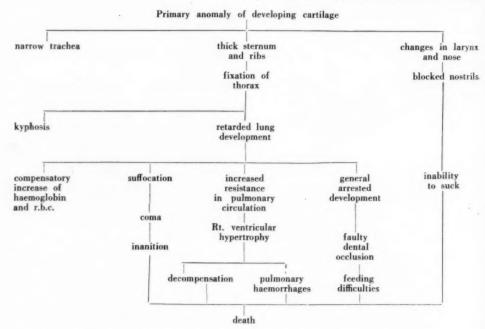
It must be realized that since both genetically and environmentally produced anomalies arise by interference with normal processes at a given age for each anomaly it is not possible by mere inspection of the case to distinguish between them. For example, considering hereditary cleft palate as the genotype, it is possible experimentally to produce in normal stock (by deprivation of vitamin B2) a "phenocopy" indistinguishable clinically from the genotype, since in both the mechanics of production, the formal genesis (i.e., failure of the palate folds to meet at the right time) is the same. A detailed history both of the family pedigree and of the individual pregnancy history is therefore essential if we are to try to distinguish between the genotype and its phenocopy, on which distinction is, of course, based our prognosis for future pregnancies.

In studying the causal genesis of defects we can gain much information from animal experiment. We now know that the genes tend to act as biochemical units, enzymes mediating a particular physiological process and therefore influencing a particular tissue development throughout the body rather than that of a particular organ. If, however, they come into action before histo-

genesis has occurred, (for example when the dorsal lip of the blastopore shows abnormality) anomalies of gross structure rather than of tissue may result. In the main, however, they determine tissue anomalies, though these may lead to results in which the original tissue defect may not be immediately apparent. An example of this can be seen in a certain strain of rats carrying a lethal gene whose primary action is to produce an anomaly of cartilage but whose apparent effect is to cause death from decompensated heart disease, pulmonary haemorrhage and starvation. The following "pedigree of causes" (after Grüneberg) demonstrates how the secondary and compensatory effects may completely overshadow the actual genetic fault:

bizarre set of anomalies is somewhat closely paralleled in Little and Bagg's disease of mice (also known as myelencephalic blebs) in which a delayed closure of the foramen anterius allows of the passage of cerebrospinal fluid into the subcutaneous tissues, whence it may seep to different parts of the body, producing deformities of the eyes, of the skeleton of the fore and hind paws, of hair distribution and of certain internal organs, especially the kidneys. A study of the formal genesis (by sectioning a series of embryos of the affected stock) of such genetic anomalies does much to demonstrate the incompleteness of the older theories of causation which refer the anomaly to involvement of a germ layer or a single organ primordium. Even the studies of von Szily

Primary anomaly of developing cartilage

narrow trachea   thick sternum and ribs   changes in larynx and nose

fixation of thorax   blocked nostrils

kyphosis   retarded lung development

compensatory increase of haemoglobin and r.b.c.   suffocation   increased resistance in pulmonary circulation   general arrested development   inability to suck

coma   Rt. ventricular hypertrophy

inanition   faulty dental occlusion

decompensation   pulmonary haemorrhages   feeding difficulties

death

In a strain of mice Grüneberg has described a transitory cartilage anomaly which shows itself later in altered shape of the skull leading to anomalies of the eyelids and of the distribution of the sensory hairs of the face. This sort of thing must be taken into account when attempting to understand multiple and apparently unrelated anomalies in man such as are found for instance in the Laurence-Moon-Biedl syndrome. This

at the beginning of the century on the formal genesis of coloboma of the choroid and of orbital cysts and microphthalmia in rabbits showed us that the clinical end-result may not resemble at all, or even supply a clue to, the condition of parts at the beginning of aberrant growth. For example, sections of the intercalary membrane of a coloboma of the choroid from an adult give no indication of the now well known fact that during

embryonic life the membrane consists of a double layer of retina with the visual elements of each opposed to those of the other. Secondary degeneration due to failure of the choroidal blood supply (itself associated with absence of the retinal pigment epithelium) accounts for the adult picture, and the ultimate genetically determined aberration is seen to be an excessive eversion of the inner layer of the optic cup before closure of the foetal fissure, and not a failure of this to close, as might easily have been surmised from an examination of adult stages alone. We thus see that detailed study of the formal genesis of genetic defects in animals is essential to the elucidation of anomalies in man, in which the early stages are not available.

Many stocks of animals carrying hereditary defects are now available, for example, those in the following list:

Pig	Microphthalmia
Mouse	Cataract
	Anophthalmia
	Open lids
	Coloboma with albinism
	Myelencephalic blebs
	Corneal opacities and "fidget"
	Rodless retina
	Anterior eye anomalies
	Recessive rupture of the lens
Rat	Microphthalmia
	Retinal degeneration and cataract
	Cataract
	Bee-swarm cataract
	Bent-nose and vitamin D deficiency
Cavy	Microphthalmia
	Corneal anomalies
	Doyne's discoid cataract
Rabbit	Coloboma of choroid
	Buphthalmos
	Microphthalmos with orbital cysts
Man	Identical twins with pinguecula, pterygium, arcus senilis, iris changes, macular degeneration, cataract, etc.

The phenocopies of the commoner genetic defects and other sporadic defects not known ever to be genetically determined (such as the rubella syndrome of cataract, deafness and cardiac malformation) can also be studied experimentally. The earliest experiments on the influence of environment were begun by biologists and embryologists nearly a hundred years ago and their general conclusions still stand. A variety of sub-lethal noxious stimuli can be used to interfere with a developing ovum. Among those first studied were alterations of salt content, organic and inorganic poisons, radiational, thermal and gravitational stimuli, and alterations of nutrition. Infection and endocrine imbalances can also be shown experimentally to affect development. In all the experiments, however, it is apparent that the result produced on the embryo is specific for the time at which the noxious stimulus is applied and not for its nature. Thus the developing frog's egg will produce anencephalic or anophthalmic or cyclopic monsters from the same or from different stimuli provided that these are applied at the precise moment when the primordia involved (fore brain, optic pits and mesial nasal process respectively) are just appearing. If applied after the head has formed they will produce deformities towards the caudal end and if applied after organogenesis is complete no structural defect will result. In other words only cells in active mitosis are affected. Table I shows the various effects produced by application of X-rays to pregnant mammals at varying times.

TABLE 1.

Animal	Day of development at which X-rays applied	Result
Rat	9th day	Hydrocephalus
	10th day	Ocular abnormalities
	11th day	Malformed jaws
Rabbit	9th-15th day	Retinal rosettes
Mouse	7th day	Resorption of embryo
	8th day	Meningocoele
	9th-14th day	Kinked or short tail
	12th-14th day	Hydrocephalus
	14th-17th day	Sterility
	18th-19th day	Cataract
Man	6th week	Retinal rosettes

TABLE 2.

Animal	Effect of infection or haemorrhage at	Result
Man	2-7 weeks 2-8 weeks 9-15 weeks	Mongolism Cataract, deaf mutism, mental and cardiac defect Encephalo-ophthalmic syndrome

The only thing which can produce a congenital anomaly when applied late in development is disease. In mammals and man it can be shown that the foetus in utero can suffer from infectious disease transmitted from the mother via the placenta in the later months of pregnancy. It may then be born with obvious lesions, such as healing small pox pustules or corneal ulcers. The earlier in the pregnancy the disease of the mother occurs the less will the effect on the embryo resemble the disease and the more it will be specific for the time of infection. This is shown by the reports of the effects of rubella and of uterine haemorrhage (Table 2). Table 3 shows in the form of a graph the time relation between maternal illness and foetal abnormality.

Nutrition of the mother during pregnancy or even before conception (in the case of chickens for example) may exercise a profound effect on the offspring. It is known that vitamin A deficiency in the mother can produce xerophthalmia and optic atrophy in the young, that B2 deficiency will lead to cleft palate and syndactyly and that vitamin B deficiency in certain strains of rats will lead to a facial malformation called "bent-nose." This only occurs if the genetic constitution is such that the embryo will react in this way and is not common to all strains of rats. It is an example of a genetically determined but environmentally produced anomaly and may be paralleled by sickle cell anaemia in negroes. 7.3 per cent. carry the genetic tendency but only 2 per cent. of these develop the anaemia, an environmental factor not always present being necessary as well.

Deficiency or excess of trace elements may also affect development of genetically normal embryos. Copper deficiency leads to "sway back" in new born lambs and selenium excess to skeletal defects in chickens. In man iodine deficiency in the mother produces cretins.

Infections of the mother during the organogenetic period are known to produce deformities in the offspring. Since the outstanding work of Australian observers on the effect of rubella other reports of similar cases associated with variola, virus influenza and tosoplasmosis have appeared.

FAMILY PROGNOSIS.

It is now obvious that in order to answer the parents' questions "Will subsequent children also be affected?" and "Will the descendants of this child show the defect?" we must endeavour to make up our minds as to the causal genesis. To do this satisfactorily it is necessary to compile
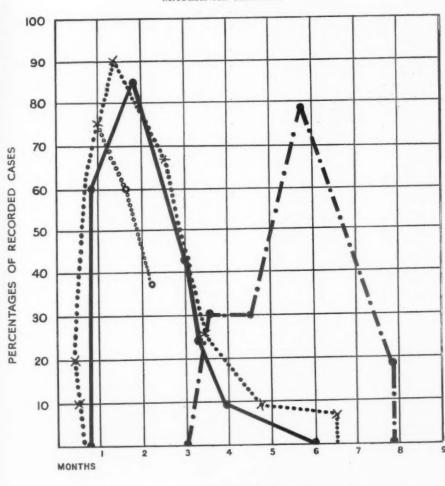

FIG. VII. Family showing dominance of ptosis and epicanthus.

DI

a fam
and de
of the
should
pregna
concer

TABLE 3.

DIAGRAM ILLUSTRATING THE OCCURRENCE OF ABNORMALITIES WITH MATERNAL ILLNESS.

CATARACT AND RUBELLA

MONGOLS AND HAEMORRHAGE

MONGOLS AND RUBELLA

ENCEPHALO - OPHTHALMIC SYNDROME
(Haemorrhage and Infection)

a family tree with details of all defects and deformities. If any comparable with that of the patient are found, those individuals should be examined if possible. A detailed pregnancy history should be taken, especially concerned with the first six months and extending a month before the pregnancy was supposed to have started. Full details of ante-natal treatment, of any febrile illness whatever, even coryza, or of contact with any infectious disease should be asked for. Details of physical injury, mental shock

or worry sufficient to interfere with nutrition or endocrine balance should also be noted. Actual tests, such as those for toxoplasmosis may be necessary. In many cases it will then be possible to give a definite prognosis for future pregnancies. If the cause appears to be environmental this is good, as safeguarding will be possible and often, as in the case of rubella, cannot occur again. In genetic defects the answer must be more guarded but the pedigree may reveal a frank dominance and the defect may be one whose genetic behaviour is well known. In cases where no cause can be assigned the possibility of a mutation having occurred by a fortuitous mating must be pointed out, as all hereditary defects must have had a beginning in the affected families.

So far we have been apt to concentrate too much on the hereditary aspect of developmental defect, but with modern work on the role played by maternal disease in the early months of pregnancy in producing abnormalities it becomes obvious that it is equally necessary to inquire in detail for the pregnancy history and that ante-natal care to be effective must begin much earlier than is usually thought necessary.

TRANSPLANTATION OF URETERS INTO THE COLON.

By GRAYTON BROWN.

Melbourne.

INTRODUCTION.

THE great improvement in the chemothera-peutic agents for cleansing the large bowel has completely changed the complexion of large bowel surgery in recent years. Uretero-colic anastomosis is one of the operations which can now be regarded as a reasonable risk for a patient who requires diversion of urine from the bladder.

HISTORICAL.

Most investigators agree that the first operation of this description was carried out in 1851 for exstrophy of the bladder (Simon, 1852). Simon planned to pass a silk seton type of suture through the exposed ureteric orifices into the rectum. A part of the original description of the operation warrants quoting:—

"On Saturday, 5th July, 1851, the patient was brought into the theatre and placed under the influence of chloroform. Mr. Simon introduced a catheter containing a thread-bearing stilet into the orifice of the ureter, and having carried it on for the proper and previously ascertained distance, while the instrument was kindly held by Mr. Green, he endeavoured by gently pressing and working the handles of the spring stilets to effect the above described operation.

The patient died of debility twelve months after the operation.

This case testifies the ardent wish of the surgeon to benefit his patient but that the risks are perhaps disproportionate with the annoyance of the malformation."

Transplantation of ureters into the colon was first attempted in 1878 (Smith, 1879) by an extra-peritoneal approach, again using a seton type of suture. The patient died after the second ureter was attacked and the kidneys were found to be grossly infected. Chaput (1892) carried out an end-to-side anastomosis of ureter and colon.

Maydl (1894) transplanted the intact trigone into the rectum in cases of ectopia vesicae. The operation was not successful in the several cases he attempted owing to high mortality and fistula formation.

Bergenham, quoted by Buchanan (1909), through an extra-peritoneal approach, implanted each ureter, into the rectum. This operation was carried out in Adelaide in 1899 (Lendon, 1906). It became known as the Lendon-Peters operation in the English speaking world, Peters being a Canadian surgeon.

Fowler (1897) attempted to protect the opening of the implanted ureter inside the bowel, by manufacturing a flap of colonic mucosa which would cover the ureteric opening during the passage of faecal matter. The results of this operation were not satisfactory.

Until 1907, all implantations took the form of a direct anastomosis between the ureter and the colon, end-to-side or even side-to-side.

Between 1907 and 1911 both Stiles (1911) and Coffey (1911) reported successful cases, using an oblique implantation of the ureter into the colon. In reviewing previous case reports, Coffey (1911) found that the majority of patients had died as the result of renal infection and all had gross dilatation of ureters. Furthermore, when working on the implantation of the common bile duct into the duodenum of experimental animals, he found that if a simple end-to-side anastomosis was carried out, the common bile duct invariably became very dilated and infected. He concluded that this was the result of peristalsis in the bowel forcing fluids or gases into the unguarded common bile duct. He then devised

a simple flap valve arrangement to prevent this periodic high pressure affecting the common bile duct by implanting the duct obliquely through the bowel wall so that it ran for some distance between mocosa and muscle layers before entering the bowel lumen. He utilised this principle for implanting ureters into the colon and I believe this simple procedure was the greatest advance in the operation. However, the site for implantation chosen by Coffey was on each side of the rectum, which made the operation technically difficult and dangerously fixed the rectum and the displaced ureters. The ureters were kept patent by means of indwelling catheters. Stiles (1911) enclosed the implanted ureter in a complete thickness of bowel wall.

Slight modifications of the Coffey technique were described by Mayo (1919). He kept the ureters patent by means of a small catgut wick instead of ureteric catheters.

Grey Turner (1925) described a series carried out by the Coffey technique but he abandoned any form of internal splinting of the openings of the ureters.

However, infection of the kidneys, obstruction of the ureters and peritonitis were still being too commonly encountered to make this operation anything less than a very hazardous procedure.

The experimental work done in this country by Walker-Taylor (1931) must be mentioned. He attempted to reduce the possibility of infection and peritonitis by means of a blunt dissection, burrowing a tunnel through the coats of the bowel instead of laying it open as in the Coffey method. If improved chemotherapy had not become available, his method would have been very important.

In an attempt to decrease the risk of sloughing of the ureters Flocks (1947) described a new two-stage operation which consisted of infolding the intact ureter in a fold of the bowel wall. Sloughing would then be unlikely and obstruction to urine improbable. At a subsequent operation, the ureter below the implantation was merely ligated.

With the improvement in chemotherapy of the bowel, there has been a great decrease in the mortality rates of this operation. As a result there has been a return to the simple operations which were carried out a long time ago.

Rizzi (1948) has re-introduced the Maydl operation for ectopia vesicae. Cordonnier (1949) and Nesbit (1949) now use an end-to-side anastomosis as a routine.

In reviewing the history of this operation, the most notable case is perhaps that of the patient who was suffering from ectopia vesicae and was treated by transplantation of ureters by Stiles in 1911 and was still alive and well twenty-five years later.

The most notable series of cases is that of Grey Turner (1943) who, reviewing his long term results for ectopia vesicae, found that of 17 cases operated upon, 9 were still alive, the time since operation varying from sixteen to thirty years.

GENERAL CONSIDERATIONS.

The indications for this operation are not numerous, but occur sufficiently frequently for an efficient method to be available.

In cases of carcinoma of the bladder where partial cystectomy is impracticable, transplantation of ureters can be advised without hesitation. However, diversion of urine from the bladder as a palliative measure for irremoveable carcinoma of the bladder is not advised because it does not stop the pain and strangury which are the frightful companions of a patient dying from this disease when cystectomy is impossible.

It is now generally agreed that cases of ectopia vesicae are best dealt with by transplantation of ureters into the colon. The best results of transplantation are in these cases, and Grey Turner's series (1943) are quite remarkable. Plastic procedures such as described by Pickerill and Pickerill (1945) are very tedious and the end result unsatisfactory compared with that where transplantation has been carried out.

In severe tuberculous cystitis transplantation of ureters into the colon may give an unfortunate patient some comfort in his few remaining years. The operation has been carried out for cases of Hunner's ulcer and intractable chronic non-specific cystitis producing a small bladder and extreme frequency of micturition.

Irreparable vesico-vaginal fistula, especially when resulting from excessive radiotherapy cannot be controlled satisfactorily with the various rubber appliances which have been advised from time to time and are most suitable for uretero-colic anastomoses. In cancer of the prostate and upper urethra, transplantation of ureters with abdomino-perineal cysto-prostatectomy may be the only method of performing radical excision of the growth.

The blood supply of the ureter is also an important study in this operation. This has been carefully investigated by Michaels (1948) who demonstrated several very useful points. The blood supply is ultimately from a peri-ureteric vascular plexus which is itself supplied by branches of the inferior vesical, internal iliac, common iliac, spermatic or ovarian, and renal vessels. The branches from the common iliac arise near the bifurcation of the aorta and are long vessels.

This is an important factor in the method about to be described because the main branches to the lower end of the ureteric plexus from the inferior vesical and internal iliac vessels may be ligated and, provided the plexus itself is preserved by wide dissection, the ureter may be freed up as far as the common iliac vessels without endangering the blood supply of its freed lower end, which is about 2½ inches long.

A further point for discussion is whether the operation should be carried out in two stages—one ureter being transplanted on each occasion or both ureters transplanted at the one sitting. It is considered that both ureters may be transplanted at the one operation with reasonable safety. Furthermore, if the patient is in good health, additional procedures such as total cystectomy may also be completed at the same time.

The principles of the present method are as follows:—

1. Careful pre- and post-operative preparation of the bowel to diminish infection at the site of the implantation.

2. R o u t i n e intra-venous alimentation during and after operation. The anaesthesia is best produced by using pentothal induction followed by cyclopropane assisted by curare.

3. The point where the ureters are most accessible is at the level of the bifurcation of the aorta, and in order to bring the bowel up to this point, the mid-sigmoid colon must be used as the site of the implantation.

4. The Coffey valve technique is used to protect the kidneys and ureter from infection due to influx of gas and colonic content during peristalsis, and also because it is simple and easier to perform than an end-to-side anastomosis, although the latter method is gaining popularity.

DETAILS OF PRE-OPERATIVE PREPARATION.

Renal function is measured as accurately as possible by means of urea clearance tests and intra-venous pyelograms. In several cases, with poor renal function before operation, after the ureters were transplanted into the colon and were no longer subjected to the pressure of a carcinoma, or the infection of chronic cystitis, the renal function improved remarkably. It is preferable to rely upon clinical judgment to determine whether the patient can survive the long operation.

Intra-venous pyelograms are also necessary to determine the presence of anomalies of the ureters. It would be embarrassing to find a leakage of urine from a third ureter after the other two have been successfully transplanted. Jacobs (1946) has reported a surprisingly high incidence of double ureters encountered in carrying out this operation.

If the urine is infected, sulphacetamide 13 g. daily should be prescribed; some authors prefer the mixed sulphonamides. In severe infection, streptomycin 2 g. daily

may be required. If the urine is not infected, I do not use any urinary antibiotics before operation.

The bowel preparation is most important. The bacterial content of the colon should be reduced to a minimum by means of oral administration of sulphaphthalidine 3 g. daily for five days before operation and streptomycin 2 g. on each of the two days preceding the operation. In addition, the bowel is emptied each morning for these five days by means of a four-pint soap and water enema or by means of a thorough bowel washout. After complete evacuation of the enema on the two days preceding operation, an antibiotic fluid is run into the bowel.

It contains the following ingredients:—
Sulphaphthalidine: 12 g.
Penicillin: 100,000 units.
Streptomycin: .5 g.
Sterile saline ad.: 200 c.c.

The large enema is also a test of the patient's ability to hold urine in the rectum and colon. A digital examination of the anal canal gives an indication of the degree of anal control in most cases, but the enema test is most re-assuring.

A full diet rich in calories and vitamins is given until forty-eight hours before the operation, when the residue is reduced to a minimum.
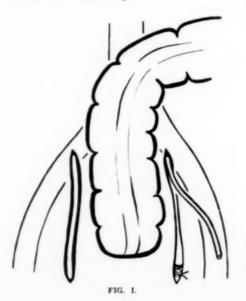
A haemoglobin estimation is carried out, and if below 70 per cent. it is brought up to at least 90 per cent. by preliminary transfusions. If, however, it is above 70 per cent. then restoration is commenced just before operation.
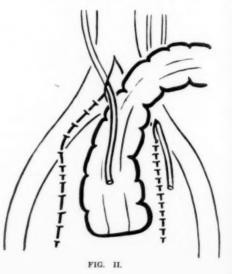
TECHNIQUE.

A continuous drip of 5 per cent. glucose in water is established into a forearm vein immediately before the operation, blood being substituted if necessary. This is continued for at least two days after operation, at the rate of four litres per day, the constituents varying from glucose in water, glucose in saline, or blood as indicated.

The patient is placed in a moderate degree of the Trendelenberg position on the operating table. It is necessary to have a skilled assistant and two fully trained sisters in charge of the packs and instruments.

A horizontal incision is carried out midway between the umbilicus and the pubis, and the rectus abdominis muscles are divided completely. The inferior epigastric vessels are then divided between ligatures and the

FIG. I.

FIG. II.

peritoneum is opened by a horizontal incision. A self retaining retractor is not required with satisfactory anaesthesia.

The small bowel and caecum are lifted from the pelvis and retained under the upper flap with large packs.
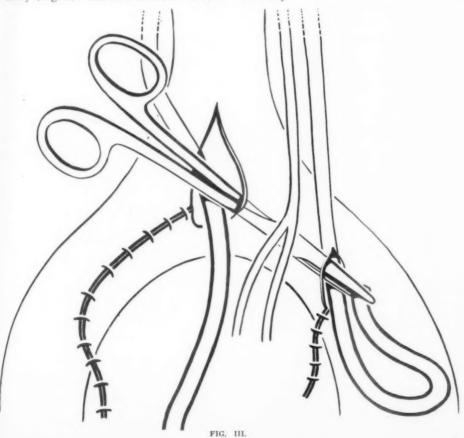
The sigmoid colon is then freed from the left iliac fossa by separating the fold of parietal peritoneum from the sigmoid mesocolon. This colon is then controlled by the assistant.

The right ureter is identified as it shows up through the peritoneum, small waves of peristalis being useful in identifying it. The overlying peritoneum is then incised in the line of the ureter from the floor of the pelvis up to the level of the right common iliac artery (Fig. 1). The incision is then directed

upwards and medially to the midline in front of the aortic bifurcation (Fig. II). The right ureter and peri-ureteric plexus are then freed *en bloc*, taking care to divide the feeder vessels from the internal iliac vessels well away from the plexus.

The branches from the common iliac vessels arise from the medial aspect and are quite long. They may therefore be preserved intact as the upper end of the ureter is displaced about half an inch towards the midline.

The lowest aspect of the ureter which is about half an inch from the opening of the bladder, is then clamped and the distal stump ligated. There is very little flow of urine from the proximal end but a continous toilet of the peritoneum with a sucker is necessary.

FIG. III.

The left ureter is similarly ligated, divided, and freed up as far as the sigmoid mesocolon which is at the level of the left common iliac artery at this point. It is then delivered through the upper part of the right peritoneal incision by means of blunt burrowing with a finger, and later by means of a Moynihan's forceps (Fig. III). The left ureter is displaced half an inch towards the midline by liberating it on the lateral side with the finger, so preserving the long branches from the left common iliac vessels. This means that the left ureter is brought across behind the inferior mesenteric vessels. This is preferable to bringing the left ureter through the sigmoid mesocolon, because it enables the ureters to lie in the same plane and be implanted close together. The sigmoid colon may later be fixed to the parietal peritoneum in one spot only, which is preferable to fixing it in addition to its own mesocolon around the left ureter.

The two ureters then lie symmetrically about the midline approximately 1½ inches apart, with about 3 inches of freed ureter and ureteric plexus available for implantation (Fig. IV.)

The apex of the loop of sigmoid colon is selected for the site of implantation because it is most mobile and may be taken to the point where the ureters emerge from their normal positions behind the parietal peritoneum and firmly sutured to this point.
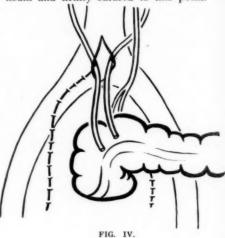

FIG. IV.
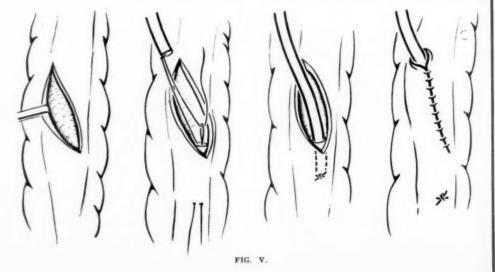
The taenia nearest the mesenteric border is selected and after silk guy sutures have been inserted, an oblique incision 1½ inches long is made through the muscle coats exposing the mucosa which is freed a little on each side to produce sero-muscular flaps and create a loose bed for the ureters (Fig. V).

There is very little bleeding from this incision, which is evidence against the assertion by Davalos (1947) that a longitudinal

FIG. V.

incision interferes with the blood supply of the colon and that, therefore, he favours a circular incision.
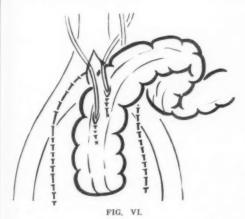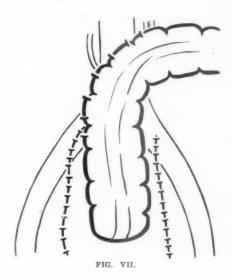
The mucous membrane is opened at the lowest aspect of the incision. The end of the left ureter is transfixed with a suture of 00 chromic catgut, leaving both ends long. Using a straight round-bodied needle, these two ends are in turn passed into the lumen of the colon and out again through the bowel wall about $1\frac{1}{2}$ inches below the mucosal opening. When these ends are tied, the end of the ureter is fixed in the bowel lumen $1\frac{1}{2}$ inches below the opening in the mucosa. The sero-muscular flaps are then sutured over the ureter so that it lies in a mucosal bed. Interrupted sutures, using an atraumatic needle, are used. It is imperative that none of these sutures pass through the ureter, although this has been advocated by many surgeons. The only fixation suture for the ureter must be the one through the extreme tip, already described. Many cases of peritonitis after the operation were caused by these transfixing sutures.

The interrupted sero-muscular sutures are inserted so as to avoid compressing the ureter, particularly at the upper end where it enters the mucosal bed.

FIG. VI.

The right ureter is similarly implanted immediately below the fixation point of the left ureter (Fig. VI). This portion of the colon is then sutured to the parietal peritoneum around the opening through which the ureters emerge, using interrupted sutures (Fig. VII).

FIG. VII.

During these manoeuvres there may be a good deal of puckering of the colon with invagination of the fixation point, due to the tension of the ureter. However, the end result, when the bowel is sutured to the posterior wall of the abdomen, is a ureter which enters the bowel in an extra-peritoneal plane, with only about $\frac{1}{2}$ inch of its length outside the bowel wall which has been disturbed from its normal bed. There is a further 1 or $1\frac{1}{2}$ inches embedded in the bowel wall with the bowel mucosa acting as a flap valve, and a further 1 or $1\frac{1}{2}$ inches inside the bowel lumen (Fig. VIII). The extreme tip of the ureter is the only fixed point. No other suture passes through the ureter. As a result, the ureter takes up its final position, without kinking and without tension.

Some of the intra-colonic portion of the ureter may slough owing to deficient blood supply, although this is unlikely. Even if sloughing should occur, the tensile strength of the dead portion of the ureter will be sufficient to anchor the ureter well past the time when fusion between the ureters and bowel wall has occurred. Some surgeons consider that this sloughing causes a stricture at the point where the slough separates, but post-mortem examinations reveal that the intra-colonic portion of the ureters resembles a small rosette without any evidence of stricture of the central orifice.

The abdomen is then closed without drainage. A rectal tube is inserted about 3 inches inside the anal canal, and is later connected to a bedside bottle.
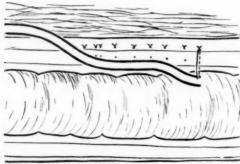

FIG. VIII.

POST-OPERATIVE CARE.

The routine as for operations on the colon is advisable. All fluids for twenty-four hours are administered intravenously. Morphia is given strictly four hourly, in order to rest both the patient and the colon. Urine usually appears through the rectal tube within twelve hours, although in one case it did not appear in any quantity for twenty-four hours. The tube must be removed daily and cleaned before replacing.

Fluids by mouth are given during the second day and increased gradually if they are tolerated well, the intravenous administration stopped.

Sulphaphthalidine and sulphacetamide (3 g. each) are given daily, commencing on the third day when the fluids taken by mouth should be at least 80 ounces.

Penicillin, 100,000 units and streptomycin, 1 g. is given in a combined injection every eight hours for the first four days prophylactically.

A light diet increasing with the patient's desires is permitted after forty-eight hours.

The rectal tube is withdrawn after four days. No aperient is required. The patient is encouraged to sit out of bed on the fifth day and to visit the toilet for passing urine. During the first few nights it is advisable to have a pan available at the bedside, as the desire to pass urine may be urgent and frequent, and incontinence has occurred occasionally during this post-operative period.

These patients are usually able to attain a six hour interval between acts of urination before the fourteenth day. They must be warned of the difficulty in distinguishing fluid and flatus to avoid discouraging bed-wetting.

It is extraordinary how keen these patients become in controlling their urine with the anal sphincter, and how proud they are in declaring their maximum interval between successive passages of urine.

Oral chemotherapy by mouth is discontinued after fourteen days.

COMPLICATIONS.

Anuria is possible, particularly if compression with the seromuscular sutures has occurred. The continuous administration of intravenous fluid is important, particularly for those surgeons who do not care to permit free fluids orally in the first twenty-four hours after bowel operations.

With the method described, peritonitis is very unlikely.

Acute ascending pyelonephritis is now infrequent. This complication was very common in earlier series of cases; the great improvement is due to the chemotherapy for the large bowel which is now available. Grey Turner and Saint (1936) consider that if pyelonephritis does not occur in the immediate post-operative period, it should never be troublesome later.

In most cases there has been some evidence of hydronephrosis of varying degree, but in only a few has this been severe. The presence of a degree of hydronephrosis is not a serious complication because it is common for cases of idiopathic hydronephrosis to carry on an unimpaired existence with persistent dilation of the pelvis of the kidney. Grey Turner and Saint (1936) considered that hydronephrosis was a common complication but in Turner's long term cases this condition has persisted without apparent effect on the general health.

There does not, therefore, seem to be any reason for alarm when this complication is encountered.

MORTALITY.

In twelve cases, there has been one operative death. This was the result of bronchopneumonia following a burst abdomen on the eleventh post-operative day. The transplantation appeared satisfactory at autopsy and there was no sign of renal infection or dilatation.

There have been four deaths which were not the result of the operation. Two were due to skeletal metastases in cases with very advanced carcinomata of the bladder, which had been removed by total cystectomy. One died as the result of a cerebral haemorrhage which was apparently unrelated to the operation. At autopsy the transplantation was quite satisfactory—there was no dilatation of the pelvis or ureters, and no infection of the kidneys or ureters. The cortex of the kidney was very thin, this was attributable to generalized arteriosclerosis. In the fourth case the cause of death which occurred at home eleven months after operation could not be ascertained.

The other seven cases are alive and well, but, of course, there is no significant survival period as yet.

THE CLOACAL LIFE.

These patients suffer very little discomfort. Most males state that except for assuming the sitting posture for passing urine, they notice no disturbance in their daily life.

Frequency of passing urine is the only disability. Few patients can avoid passing urine less frequently than every six hours. This, of course, is not a serious complaint.

All patients have complete control of the anal sphincter, and there is no case of incontinence. Most patients limit their fluids after the evening meal, so that they may have eight hours uninterrupted sleep. Only one patient has to get up during the night to pass urine but his general condition is poor owing to active pulmonary tuberculosis.

These patients have difficulty in distinguishing flatus from urine but as urine and flatus are being passed every six hours, this is not a serious complaint.

It is reasonable to claim that these patients have a far more comfortable life than patients with satisfactory colostomies. Apart from some frequency, their habits are not disturbed.

CONCLUSION.

I believe that using the principle of bringing the bowel to the ureter, the past difficulties of leaking of urine, sloughing of ureters and obstruction at the site of implantation, have been minimized.

The great advances in chemotherapy have practically eliminated the problem of ascending infection. This is the greatest advance in all surgery of the large bowel. As a result, the operation of transplantation of ureters into the colon has a reasonably low operative mortality.

The long term results of others indicate that the morbidity rate is also very low.

This operation is not now a formidable procedure, and should be carried out in patients when diversion of urine will assist their disease.

SUMMARY.

1. The history of the operation of transplantation of the ureters into the bowel has been reviewed.

2. Careful pre-operative preparation of these patients is emphasised.

3. An operative technique has been described in detail.

4. The mortality and morbidity of this operation is shown to be reasonably low.

5. The cloacal life is described.

ACKNOWLEDGEMENTS.

The low operative mortality is due in no small part to the care in resuscitation by Dr. E. B. Drevermann and the anaesthesia carried out by Dr. Bridges Webb.

REFERENCES.

CHAPUT, (1894), *Arch. gén. Méd.*, vol. 173, page 1.

COFFEY, R. C. (1911), *J. Amer. Med. Assoc.*, vol. 56, page 397.

CORDONNIER, J. J. (1949), *Surg. Gynec. Obstet.*, vol. 88, page 441.

DAVALOS, A. (1947), *J. Urol.*, vol. 57, page 701.

FLOCKS, R. H. (1947), *Canad. Med. Assoc. J.*, vol. 56, page 259.

FOWLER, G. R. (1906), "Treatise on Surgery." Philadelphia and London. W. B. Saunders & Co., vol. 2, page 313.

JACOBS, A. (1946), *Brit. J. Urol.*, vol. 18, page 4.

LENDON, A. A. (1906), *Brit. Med. J.*, vol. 1, page 961.

MAYDL, K. (1896), *Wien. med. Wschr.*, vol. 46, page 28.

MAYO, C. H. (1919), *Osler Memorial Volume.*

MICHAELS, J. P. (1948), *Surg. Gynec. Obstet.*, vol. 86, page 36.

NESBIT, Reed M. (1949), *J. Urol.*, vol. 61, page 728.

PICKERILL, H. P. and C. M. (1945), *Aust. N.Z. J. Surg.*, vol. 15, page 91.

RIZZI, R. (1948), *Urol. Cut. Rev.*, vol. 52, page 518.

SIMON, John (1852), *Lancet*, vol. 2, page 586.

SMITH, T. (1879), *St. Bart's Hosp. Rep.*, vol. 15, page 29.

STILES, Sir Harold (1911), *Surg. Gynec. Obstet.*, vol. 13, page 127.

TURNER, G. Grey (1929), *Brit. J. Surg.*, vol. 17, page 114.

TURNER, G. Grey (1943), *Brit. Med. J.*, vol. 30, page 535.

TURNER, G. Grey and SAINT, J. H. (1936), *Brit. J. Surg.*, vol. 23, page 580.

WALKER-TAYLOR, P. N. (1931), *Aust. N.Z J. Surg.*, vol. 1, page 158.

EDITORIAL.

SURGICAL JUDGEMENT.

IN a surgeon there is no quality of mind more to be desired than that of judgement. Judgement is the product of a mind cultured by a liberal and a professional education and matured by experience. It is judgement even more than skill that makes a truly successful surgeon.

Judgement is not readily developed during under-graduate training when the academic foundations of a surgeon are being laid. In the comparatively short period of under-graduate training, the student is required to absorb a mass of accepted knowledge, presented to him with a dogmatism characteristic of under-graduate teaching. There is too little time for explanations which would enable him to assimilate it on a basis of physiology and pathology. The intensive teaching dulls any imagination he may have; and the result is that if he is to be academically successful he must form memorizing rather than reasoning habits of mind. Thus, though he may acquire much knowledge, he develops little wisdom and lays no foundation in the art of acquiring wisdom.

As time goes on, however, the developing surgeon begins to exchange his memorizing for reasoning habits of mind. In this way he begins to accumulate that mature wisdom and develop that sound judgement which is so essential in the make-up of a surgeon. He is encouraged in this as he comes under the influence of those who have attained a position in the profession which entitles them to hand on the torch of knowledge and to point the way of wisdom and judgement. The young surgeon becomes sensible of this influence first in the hospital wards, operating theatres, and laboratories, then at surgical conferences, and finally through the medium of surgical literature, in relation to which he must cultivate a kindly critical mind.

Chastened by his experiences, enlightened by his scientific association, and encouraged by the counsels of his seniors, he develops a changing point of view. He begins to lose his rigidity of mind, to rely less on text books and more on his own observations, to have doubts, to develop an open mind, and above all to acquire a humility of thought—perhaps the greatest sign of wisdom. And then naturally come an assessment of the clinical value of his experiences; an examination of surgical procedures in the light of his developing judgement; an accumulation and assortment of these for comparison with others of a like nature in the future. Then follow speculations, inferences and hypotheses; the testing of these by further observations; and finally theories and discoveries. All these are milestones in the cultivated march of surgical judgement. If now Nature has been kind to him and his Christian and vocational roots lie deep, the end result should be the ideal surgeon.

H. B. Devine.

Books Reviewed.

ATLAS OF HUMAN ANATOMY, DESCRIPTIVE AND REGIONAL.

By M. W. WOERDEMAN, M.D., F.R.N.A.Sc. Vol. 1. London: Butterworth & Co. (Publishers) Ltd., and Amsterdam: Wetenschappelijke Uitgeverij, 1948. 6¾" x 10", viii, 512 plates plus index. Price: 82s.

Professor M. W. Woerdeman, of the Department of Anatomy in the University of Amsterdam has made a notable contribution to anatomical literature with the first volume of his "Atlas of Human Anatomy" which is devoted to osteology, arthrology and myology.

The method of presentation of his material is new and is carried out in a most pleasing manner. His illustrations of the osteology of the foetus and young child form one of the most valuable sections of the atlas. The section dealing with the skull is excellent, indeed it is doubtful if better illustrations have ever appeared in modern anatomical literature.

The attachments of the muscles are presented in a new and most refreshing manner and will prove to be of considerable value to students. The drawings of the muscles and joints are taken from dissected specimens and therefore present a very true picture of their anatomy.

The book is very well printed and produced and both author and publisher alike are to be congratulated on its format.

There are a number of errors in the labelling of some of the illustrations. These are mostly of a minor nature and are listed on an errata slip.

It is felt that the atlas will be of most value to post-graduate students of anatomy although the under-graduate will find plenty of food for instruction within its pages.

The appearance of the second volume devoted to the digestive system, the respiratory organs and the organs of the urogenital system will be awaited with considerable interest.

ALFRED HOSPITAL CLINICAL REPORTS, 1949. Vol. 1, No. 1.

Under direction of Editorial Committee. Melbourne: Alfred Hospital (Incorporated), 1949. 9½" x 6", 614 pp., numerous illustrations and tables. Price: £1 1s.

This first number of the Alfred Hospital Clinical Reports is an excellent production. It contains eleven papers including one which is divided into four parts. There is, in addition, an introductory note regarding the Alfred Hospital Clinical School.

The standard of the papers is high. The material contained in them is good and they are well presented and illustrations contained in some of them are of high technical excellence. The editors of these reports have set themselves a very high standard in this first production.

There is no question but that journals of this type have a place in medical literature but their place is in the parochial literature of a town or even a hospital rather than in the medical literature of the world. It follows that material of general interest should be published in the well-known journals of world-wide circulation. There is plenty

of material which may not be new to the world literature but may be new in a particular hospital. There are results of investigation or treatment which are interesting to people in a particular place but may not be of general importance. These, of course, are the conditions which should be discussed and should provide the material for papers such as those of Clinical Reports.

The Editorial Committee notes, in its foreword, that three of the papers have been published in other journals. It is felt that this is a retrograde step. It is too recent, since multiple publications (as carried out particularly in some parts of America) became such a nuisance that special action had to be taken to cope with them, for us to consider with other than regret the development here of a similar process. Even though the problem has been introduced from a different point of view it nevertheless remains one. In this case there is no question of any attempted deception but it would seem a great pity that time and effort should be employed in reproducing material a second time, particularly in these days of shortage of printers and paper.

Any criticisms of the desirability of the production of a volume such as this (in precisely this form) notwithstanding, the particular production discussed here is of very high standard. The paper is good; the type is very clear and well set out; the illustrations are excellent and the Committee is to be congratulated on the standard of their production.

COMBINED TEXTBOOK OF OBSTETRICS AND GYNAE-COLOGY. (For Students and Practitioners.)

Edited by DUGALD BAIRD, B.Sc., M.D., D.P.H., F.R.C.O.G. Fifth Edition. Edinburgh, Scotland: E. & S. Livingstone Ltd., 1950. 9½" x 5¾", xiv plus 1411 pp., 594 illustrations, 30 in colour. Price: 70s. net.

In its fifth edition since 1923 Dugald Baird of Aberdeen has reproduced the combined textbook in rejuvinated form. To do this he has rearranged and enlarged his team to include no less than 14 other eminent contributors, all having associations with one of the three Scottish Medical Schools. He has achieved the aim of a good textbook; without redundancy to completely cover a section of knowledge, making it presentable to the eye and at the same time well knit in logical sequence. That these objects should be achieved in a volume covering the third major division of medical knowledge, obstetrics and gynaecology, is a credit to himself and the publishers.

By combining obstetrics and gynaecology in one textbook their essential unity is stressed, and the common fields of anatomy, physiology, and embryology do not require repetition. The continuity is gracefully preserved by a connecting chapter between the two subjects. It can be said that reproduction is merely an incident, though an important one, in the gynaecological lifetime of the woman, and much that is gynaecological is a legacy of obstetrics. Abortion, pelvic inflammation, ectopic gestation and infertility are here seen in their proper perspective. The book conduces to a

broader outlet on the specialty. The only criticism might be that a book so comprehensive in scope, now necessitating enlargement to over 1,400 pages, has the inherent disadvantage of being unwieldy to handle.

It is refreshing to find there are sections on the male reproductive organs, that the part played by the male in infertility receives adequate discussion, there is some mention of contraceptives, and quite a deal about the psychological states. This latter section emphasizes the expanding importance of psychosomatic medicine in relation to the genitalia. The gynaecologist is no longer essentially an operator.

The section on breech presentation is good, and Lovset's manoeuvre for shoulder-girdle dystocia now finds a place in the standard British textbooks. With regard to types of caesarean section, the authors state that a full discussion on the choice of operation is beyond the scope of the book. By many the presentation may appear unduly biased towards the older classical operation. The book does not profess to deal with details of gynaecological operations beyond graduation level, and in general, obstetrics is more fully dealt with than gynaecology. It will be accepted as the standard textbook, from the north of Britain for students and practitioners.

THE HISTOLOGY OF THE BODY TISSUE (With a Consideration of their Functions).

By MARGARET GILLISON. Foreword by R. C. GARRY, D.Sc., M.B., Ch.B., F.R.S.E. Edinburgh, Scotland: E. & S. Livingstone Ltd., 1950. 7¼" x 4¾", xiv plus 220 pp., 103 figures. Price: 15s. net.

This is an excellent little work, whose modest claims are amply substantiated in the text. It sets out to correlate microscopic structure with physiological function, in a form particularly to suit those groups of students who pursue some of their studies in departments of anatomy and physiology, and are yet not called upon to acquire an intimate knowledge of either. With a minimum of histological detail, the links between tissue structure and function are clearly appreciated, and the many diagrams are accurate and well drawn. This book would therefore be of appreciable assistance to students of physiotherapy, physical education, and kindred subjects, and, in the words of Professor Garry's foreword, could equally well serve all students as an introduction to animal biology.

CARCINOMA OF THE LARYNX. Supplement No. 3.

By F. BACLESSE, M.D. A statistical report on cases treated with X-rays only by R. W. GUNDERSON, B.Sc., D.M.R.T., F.R.C.S.(Eng.) London: The British Institute of Radiology, 1949. 9¾" x 7¼", 68 pp., 97 figures, numerous tables. Price not stated.

This monograph includes a statistical report on cases treated with X-rays only, by R. W. Gunderson at the Meyerstein Institute of Radiotherapy, The Middlesex Hospital, London.

It was written with a two fold purpose:—
(a) To show the importance of clinical and radiological examination with respect both to prognosis and interpretation of results.
(b) To discuss the various methods of X-ray therapy of the larynx in the light of the five-year survival figures.

It does not, however, discuss the relative merits of surgery as against radiotherapy in the treatment of laryngeal cancer.

A wide range of cases amenable to radiotherapy is described including the clinical and radiological points taken note of in defining the indications for radiotherapy and in evaluating the results, the whole based on 341 epitheliomata of the larynx irradiated at the Fondation Curie in Paris from 1919 to 1940 and followed up personally by the author since 1926. Cases treated after 1940 were spoiled from the statistical and follow-up point of view by difficulties directly connected with the 1939-45 War.

Histology is not considered. The author considers that, apart from establishing a positive diagnosis, its importance in deciding prognosis and technique of treatment appears from their experience to be less than that of the clinical and radiographic features. They cannot confirm the validity of conclusions by various authors regarding indications for surgery or radiation based upon histological evidence.

The study includes only tumours arising within the larynx, it excludes those arising on and outside the boundaries of the vestibule of the larynx, these latter, called "marginal" tumours (e.g., on the free margin of the epiglottis, the pharyngeal surface of the aryepiglottic fold and the posterior part of the arytenoids), are grouped with the hypopharyngeal neoplasms. Tumours are defined both by clinical (i.e., laryngoscopic) examination and by antero-posterior and lateral X-ray views of the larynx. Tumours irradiated from external fields regress centripetally and the last part of the tumour to disappear is considered to be the point of origin. By this means a relatively precise division of tumours by site of origin is made into supraglottic, glottic and sub-glottic.

Tumours, according to site, in these groups are then discussed from the point of view of diagnosis, progress of treatment (as shown by X-ray views), and also of prognosis. Excellent illustrative diagrams, sketches and photographs are given. Direction of spread of the differently sited tumours, both local and metastatic to glands is described. From the laryngologists' point of view it would seem that proper stress is laid upon the use of indirect laryngoscopy and the expert interpretation of X-rays of the larynx, the latter being particularly well described, but the valuable information both direct and confirmatory to be obtained by direct laryngoscopy using Jackson's direct laryngoscope is hardly mentioned, in fact, is not specifically mentioned at all.

Three important points in technique of treatment are stressed:
(a) The size of the field should be the smallest which will cover the tumour adequately; this may, in some cases, be reduced in size as the growth shrinks during treatment.
(b) The dose, which must be increased in the case of radio-resistant tumours and cases of glandular involvement.
(c) The total duration of treatment which they think must be increased above the generally accepted limits when very large doses are given.

The use of teleradium has been given up because of poor results. The deep X-ray technique is based upon the work and results of Coutard, the former director of the Fondation Curie.

The guiding biological principle is to avoid reactions, but nevertheless to increase the total dose. This leads to protraction of treatment and diminution of the size of the fields.

Physical factors in technique are described. Gunderson's statistical survey follows. The monograph, as a radiotherapeutic contribution is valuable but must be viewed in its proper perspective in that it does not give the full picture of the treatment of cancer of the larynx.

In the reviewer's opinion surgery has a very important place in treatment especially in cancer of the true cord and early sub-glottic and ventricular lesions.

Provided this is kept in mind there is much of value to be gleaned from the monograph.

ADVANCES IN SURGERY. Vol. II.

By WILLIAM DeWITT ANDRUS, *et al.* together with Members of Editorial Board. New York and London: Interscience Publishers, Inc., New York; Interscience Publishers Ltd., London, 1949. 9" x 5¼", xii plus 590 pp., numerous illustrations and tables. Price: $11.00.

This second volume in the series contains eleven comprehensive articles each written by an expert in his subject. These articles vary in length from forty to sixty pages and provide a useful review of various current surgical problems. Pulmonary function studies in relation to chest surgery are discussed by Riley and Cournard. Advances in surgery of the oesophagus are discussed by Sweet and an excellent survey of the treatment of hypertension is provided by Smithwick. A. O. Whipple writes on portal bed block and portal hypertension. Surgery of congenital anomalies of the heart and great vessels is reviewed by Geo. H. Humphreys. Recent advances in the treatment of cranio-cerebral injuries are well surveyed by Walker and Fisher. Use of Streptomycin in the treatment of surgical infections is covered by Pulaski, and advances in skin grafting by Bradford Cannon and J. B. Brown.

"The Pathology of Tumours of the Peripheral Nerves," by N. C. Foote, and "Testis Tumours," by Lloyd G. Lewis are again both excellent. These two articles are really monographs on subjects in which a great deal of experience has accumulated over a long period in a laboratory of surgical pathology or under the extraordinary concentration of cases during the war. Lewis bases his views on primary neoplasms of the testis on material obtained from approximately 1,000 testis tumours examined by the Army Institute of Pathology during a five year period from an army of about 10,000,000 men, an incidence of 1 in 10,000 men.

Advances in the management of pancreatico-duodenal cancers by C. G. Child provides a chronology of the significant features in the development of the radical operation for these conditions from 1935 onwards and concludes with a good survey of the position in 1949. Although radical surgery at present offers the only chance of cure for these difficult problems the survival periods in patients so operated on is discouragingly short and raises the question as to whether or not radical pancreatico-duodenectomy should be performed at all for pancreatic cancer.

This book can be well recommended as containing a very useful set of articles each of which is supported by numerous references.

ESSENTIAL UROLOGY.

By FLETCHER H. COLBY, M.D. Baltimore, U.S.A.: The Williams & Wilkins Company, 1950. 9" x 5¼", vii plus 580 pp., 342 illustrations. Price: 86s. (Sent by Angus & Robertson Ltd., Sydney.)

This short text book on basic urology, is designed primarily for medical students and recent graduates. It includes a comprehensive section on anatomy and embryology; also a section on the manner of examination and investigation of genito-urinary conditions.

The remaining portion is on the diseases of the genito-urinary organs, with most of it devoted to etiology and diagnosis. Basic treatment only, is included.

It is not a comprehensive text book on urology. It will be found an extremely useful work for final year medical students.

All chapters are well illustrated, with drawings, photographs and specimens and reproductions of X-ray pictures.

The book, as a whole, is well set out and easy to read.

THE BREAST. Structure: Function: Disease.

Edited by F. D. SANER, M.B., B.Ch.(Camb.), F.R.C.S. (Eng.). Bristol: John Wright & Sons Ltd., 1950. 6" x 9", xii plus 316 pp., 193 illustrations. Price: 45s.

This is a book written by fifteen authors. Mr. Saner, the editor, is joint author of a number of the chapters. All aspects of the diagnosis, pathology and treatment of lesions of the breast are discussed. There are chapters on structure and function and the abnormalities of structure and function, on examination and diagnosis, dysplasia and chronic mastitis on benign tumours and infective lesions and one on plastic surgery. There is much of interest, illustrated by numerous photomicrographs.

It is always difficult in a book, to which many authors contribute, to keep the matters in correct perspective and in this book, the editor has not altogether succeeded. This is particularly noticeable in the section devoted to carcinoma. The value of radiotherapy is over-stressed. The reader might well have expected more information concerning the place of hormone therapy in carcinoma of the breast and a fuller discussion of the present day problems of its surgery. The section on biopsy would be unacceptable to the many surgeons, who believe that the biopsy of malignant tumours should ordinarily be followed forthwith by operation.

Book Received.

NOTES ON COMMUNICABLE DISEASES OF LABORATORY ANIMALS.

By H. J. PARISH, M.D., F.R.C.P.E., D.P.H. Edinburgh: E. & S. Livingstone Ltd., 1950. 4¾" x 7¼", vii plus 69 pp. Price: 3s. net.